# Callous-unemotional traits in early childhood: developmental pathways and translation to aggression

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor of Philosophy by Nicola Wright.

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Abstract

Callous-unemotional (CU) traits have proved to be a robust and informative construct; identifying a subgroup of children with conduct problems who show more severe and persistent antisocial behaviour. The majority of this work has focused on mid to late childhood and adolescent samples, yet the study of CU traits in early childhood allows identification of developmental pathways to CU traits and may inform the development of preventative interventions. The three empirical studies included in this doctoral thesis use a longitudinal epidemiological sample (Wirral Child Health and Development Study; WCHADS) followed from pregnancy up to age 7 years to examine important questions regarding: 1) the measurement of CU traits in early childhood 2) the contribution of the early parenting relationship to child CU traits; specifically maternal sensitivity to infant distress, with possible mediation by child attachment status, and 3) a candidate sex dependant mechanism for the translation of CU traits into physical aggressive from early to mid-childhood. The first study uses the extensive sample of consecutively recruited first time mothers and the second two studies focus on a subsample stratified by psychosocial risk. The aim of the first study (Chapter 2; n = 775) was to adapt a CU traits measure for use with preschool children. The CU measure derived showed acceptable psychometric properties, factorial invariance by sex and good stability to 5 years. Validity was supported by cross-sectional associations with physical aggression for both boys and girls and incremental prediction to aggression at age 5 in girls only. The second study (Chapter 3; n = 272) examined the longitudinal contribution of maternal parenting behaviours (sensitivity to distress and to non-distress, positive regard, intrusiveness) at 7 months and attachment status at 14 months to child CU traits assessed from age 2.5 to 5 years. Latent variable modelling yielded a single parenting factor which, in line with predictions, significantly predicted reduced CU traits. The effect was mainly explained by sensitivity to infant distress and positive regard towards the infant. These two indicators evidenced a significant interaction, such that the combination of low positive regard and low sensitivity to distress predicted increased child CU traits. Neither attachment security nor disorganization predicted CU traits, so there was no evidence for mediation by attachment status. The final study (Chapter 4; n = 276) examined a hypothesised sex-specific mechanism for the translation of CU traits to aggression via HPA –axis reactivity to stress. Age 5 cortisol reactivity was found to significantly moderate the association between age 5 CU traits and age 7 teacher and mother reported aggression, evidenced by a significant 3-way interaction with sex. There was a significant two-way interaction in boys, such that higher CU traits and lower cortisol reactivity predicted increased physical aggression. Overall, this thesis provides support for the valid measurement of CU traits over the early preschool period. Sensitivity to infant distress, alongside positive regard/warmth, predicted reduced CU traits suggesting that early interventions might also focus on enhancing maternal responsiveness to distress. Findings supported the role of cortisol reactivity to social stress in the translation of CU traits to aggression and critically this was sex specific.

Declaration

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

I would like to dedicate this thesis to my mother, Pamela.

Firstly, I would like to thank my supervisors, Dr Helen Sharp and Professor Jonathan Hill for their constant support and guidance with this thesis, and for both being fantastic managers and mentors. I feel incredibly fortunate for the all the support and opportunities that they have given me over the past 7 years. I am constantly learning whilst in their presence and am very grateful to them for allowing me to become involved in the Wirral Child Health and Development Study (WCHADS). Helen has been such a supportive manager and the clinical supervision and clinical insights she provides have really helped me to develop my thinking about my work. I also want to extend a special thanks to Professor Andrew Pickles who, despite not being my formal supervisor, has given countless hours to support me with analysis and has been so patient whilst I attempt to develop a statistical knowledge that even approaches his brilliance. I have been incredibly lucky to find myself working as part of the WCHADS team and I hope to continue this for as many years as I can.

Thank you to all my friends and colleagues at First Steps. I feel so fortunate to be part of such an amazing team. Every member of First Steps works incredibly hard to keep the study going and the care and consideration shown to each other and to the families in the study are what make our team so special. Special thanks go to Dr Dr Fay Huntley, who first trained me when I started back in 2010, I learned so much from her and she has since become one of my closest friends. I feel very lucky to have worked with and become friends with Kate Abbott; her post-phd notes have been invaluable in my writing up and our conversations have always provided me with light relief! Louise Fisher, who has been so helpful and supportive and is always so calm in a crisis. Kay, who brightens up my day every time she answers the phone or is at her desk when I get in. Stu, who has put up with me bossing him around much more than usual recently but luckily he doesn't seem to resent me too much. Karen, for being so efficient and quick to help with anything you ask of her. Thank you to all past First Steppers who contributed to this thesis by giving advice, coding or collecting data: Helen, Matt, Nik, Niki, Andrea, Rachael, Becca and Florin. Finally, I am unbelievably grateful to Miriam Refberg, without her taking on so much of my work it would not have been possible to compete this thesis, I am forever in her debt. She has had to put up with mountains of emails/texts/phone calls from home whilst I've been writing up but still always had time to send me her sweet and funny replies. Special thank go to the families who take part in the WCHADS, I feel incredibly grateful that they have given up so much time to help us with the research. I have learned so much from them and have enjoyed watching the children grow up.

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## Preface

This work was conducted by the author whilst working as a full-time Research Assistant on the Wirral Child Health and Development Study (WCHADS) since the infants in the study were 14 months of age. The MRC grants for the research were awarded to Professor Jonathan Hill, Dr Helen Sharp and Professor Andrew Pickles; the co-authors on the papers included in this thesis. The author (Nicola Wright) took the lead role in the selection and oversight of administration of study measures used to assess CU traits. She also took the lead role on the second enrichment of the intensive sample at 5 years. Her main role on the study was in conducting the adult interviews and in the overall co-ordination of the child assessments for the age 5, 7 and 9 follow-ups. She conducted 43 complete child assessments at 3.5 years of age and 36 at 7 years of age, conducted 6 maternal interview assessments at age 14 months, 117 at age 2.5 years, 159 at age 5 years and 153 at age 7 years.

# Chapter 1: Background

Disruptive behaviour problems in childhood, including oppositionality, rule-breaking and aggression, are associated with a host of negative consequences, both at the individual and at the societal level. The disruptive behaviour disorders (DBD) include conduct disorder and oppositional defiant disorder (ODD) and are among the most commonly diagnosed disorders in children, with a population based survey in 1999 indicating that 5.3% of British children aged 5-15 met criteria for a DBD, with 2.9% meeting criteria for ODD and 2.5% meeting criteria for conduct disorder (Meltzer, Gatward, Goodman & Ford, 2000). Conduct disorder is defined as a repetitive and persistent pattern of behaviour in which the basic rights of others or major age-appropriate societal norms or rules are violated. Lying, cruelty towards humans or animals, and truancy are examples of behaviours included in the conduct disorder symptom profile. ODD is defined as a pattern of angry/irritable mood, argumentative/defiant behaviour, or vindictiveness. Tantrums, arguing with authority figures and blaming others for mistakes are examples of behaviours in the ODD symptom profile (American Psychiatric Association [APA], 2013). Both ODD and conduct disorder diagnosis can be applied from preschool age, but ODD is more commonly diagnosed in younger children. ODD often precedes conduct disorder but not all individuals diagnosed with ODD go on to develop conduct disorder (Frick & Nigg, 2012). Both disorders require four symptoms to meet diagnostic threshold, however, evidence suggests that individuals with sub-diagnostic levels of symptoms also show substantial impairment (Angold & Costello, 1996; Angold, Costello, Farmer, Burns, & Erkanli, 1999).

During childhood, DBD's are associated with deficits in social and familial functioning, and in scholastic achievement, and with increased risk of physical health problems and comorbid psychiatric disorders (Meltzer, Gatward, Goodman & Ford, 2003). Further, antisocial behaviour appearing in early childhood confers a substantially increased risk of later problems in adulthood such as violence, criminality, unstable relationships, and mental health problems (Hill & Maughan, 2001). Antisocial behaviour is particularly costly for society due to costs associated with criminal behaviour, extra educational provision, foster and residential care, and state benefits. One longitudinal study in the UK demonstrated that by adulthood the

costs incurred by an individual with conduct disorder were 10 times higher than that of a healthy control. In addition, individuals with conduct problems who did not meet the threshold for diagnosis incurred costs 3.5 times that of healthy controls (Scott, Knapp, Henderson, & Maughan, 2001).

There is increasing recognition that there is significant heterogeneity in conduct problems, in the risk factors, underlying processes, and behavioural expression. The identification of effective methods for subtyping conduct problems allows for the development of targeted intervention. Attempts to subtype conduct problems have included a distinction based on the age of onset of problems (Moffit, Caspie, Dickson, Silva, & Stanton, 1993) or on the types of aggression shown (i.e. reactive versus proactive; Goa, Tuvblad, Schell, Baker, & Raine, 2015). One of the most established models in the literature proposes that conduct problems can be subtyped based on the presence or absence of 'callous-unemotional traits' (CU traits). CU traits are characterised by a lack of conscience or concern for others' feelings, particularly distress, a lack of guilt and diminished emotional expression (Frick, 2009). In this thesis, three empirical papers are reported examining CU traits in early childhood. This introductory chapter will first set the broader background context for the work and give the rationale for the experimental papers that follow.

### *1.1 Subtyping conduct problems: Callous-unemotional traits*

The notion that children might display CU traits came from a downwards extension of the affective component of psychopathy, a concept which has been extensively applied to adults and found to be associated with severe and persistent antisocial behaviour (Hare, McPherson & Forth, 1988; Serin, 1991; Kosson, Smith & Newman, 1990; Leistico, Salekin, DeCoster & Rogers, 2008). Psychopathy in adults is considered to be multidimensional, comprising at least three dimensions, including affective (e.g. lack of guilt and empathy), interpersonal (e.g. narcissistic and manipulative interpersonal style) and behavioural (e.g. impulsive and irresponsible behavioural style) dimensions (Cooke & Michie, 2001). The focus on CU traits in childhood over the other psychopathy dimensions has been driven by evidence demonstrating that these traits best distinguish those antisocial children and

adolescents at high risk for early onset, pervasive, and aggressive conduct problems compared to antisocial individuals without CU traits (Frick, Cornell, Barry, Bodin, & Dane, 2003; Frick et al., 2014a). CU traits, labelled as 'limited prosocial emotions', have recently been included as a specifier for conduct disorder diagnosis in the Diagnostic and Statistical Manual (DSM V; APA, 2013). These diagnostic criteria are presented in Table 1.1. Whilst many studies do employ measures of psychopathic traits in childhood, this thesis largely focuses on studies of CU traits only. Where findings relate to a broader construct than CU traits, this will be highlighted.

**Table 1.1: With limited prosocial emotions specifier for Conduct Disorder Diagnosis is DSM V (APA, 2013)**

To qualify for this specifier, an individual must have displayed at least two of the following characteristics persistently over at least 12 months and in multiple relationships and settings.

1. Lack of remorse or guilt: Does not feel bad or guilty when he or she does something wrong (exclude remorse when expressed only when caught and/or facing punishment). The individual shows a general lack of concern about the negative consequences of his or her actions.
2. Callous—lack of empathy: Disregards and is unconcerned about the feelings of others. The individual is described as cold and uncaring. The person appears more concerned about the effects of his or her actions on himself or herself, rather than their effects on others, even when they result in substantial harm to others.
3. Unconcerned about performance: Does not show concern about poor/problematic performance at school, at work, or in other important activities. The individual does not put forth the effort necessary to perform well, even when expectations are clear, and typically blames others for his or her poor performance.
4. Shallow or deficient affect: Does not express feelings or show emotions to others, except in ways that seem shallow, insincere, or superficial (e.g., actions contradict the emotion displayed; can turn emotions "on" or "off" quickly) or when emotional expressions are used for gain (e.g., emotions displayed to manipulate or intimidate others).

### *1.2 Approaches to the study of CU traits in clinical and community samples*

As the construct of CU traits was introduced as a method for subtyping conduct problems, the majority of CU traits research has focused on clinical samples of children with antisocial behaviour. Most commonly these studies compare groups of antisocial children with and without CU traits (e.g. de Wied, van Boxtel, Matthys, & Meeus, 2012) or examine CU traits within an antisocial group and control in the data analysis for the presence of conduct problems (e.g. Pasalich, Dadds, Hawes, & Brennan, 2012). However, CU traits are increasingly studied in community samples where the focus is on the identification of predictors of the presence or extent of CU traits. Again some studies take the approach of contrasting groups of children who are high and low on CU traits or antisocial behaviour (e.g. Loney, Butler, Lima, Counts & Eckel, 2006) whereas others examine associations between variables of interest and the level of CU traits whilst controlling for conduct problems (e.g. Waller et al., 2016) or without considering conduct problems (e.g. Waller et al., 2012). Importantly, there is evidence that CU traits can occur in the absence of conduct problems (e.g. Rowe et al., 2010) and some evidence suggests that children with CU traits without current conduct problems may have worse outcomes than control children in terms of future delinquency, emotional problems, and peer problems (Frick, Cornell, Barry, Bodin, & Dane, 2003; Rowe et al., 2010 but see Eisenbarth, Demetriou, Kyranides, & Fanti, 2016). This latter finding supports the study of CU traits in their own right. When reviewing the literature in this thesis, the type of study design and sample used will be made clear.

### *1.3 Distinct correlates of CU traits*

In this section, evidence which supports CU traits as a distinct subtype of conduct problems will be reviewed. Conduct problems with and without CU traits have been referred to as ‘hot’ and ‘cold’ respectively (Dadds & Rhodes, 2008). This distinction reflects the fact that typical ‘hot’ conduct problems are characterised by high negative emotionality, particularly anger, emotional dysregulation and overreactivity, with aggression predominantly reactive in nature. In contrast, conduct problems with CU traits are thought to be characterised by low temperamental fear,

intact emotional regulation, and emotional and physiological under-reactivity, with aggression being both reactive and proactive or predatory (Frick & Morris, 2004). This theorising draws on findings from adult psychopathy which have demonstrated reduced emotional and physiological and responsiveness (e.g. Hare, 1978; Raine, 2002; Patrick, Cuthbert, & Lang, 1994; Sutton, Vitale & Newman, 2002) and deficits in processing emotion, in particular fear (Blair, Colledge, Murray, & Mitchell, 2001). Neuroimaging studies have shown associations with dysfunction in brain areas thought to be involved in the processing of emotion, mainly the amygdala (Blair, 2007). Consistent with this, findings have linked psychopathy to neurocognitive impairments that are known to be associated with amygdala dysfunction (Blair, 2006) including fear recognition, passive avoidance learning (Blair et al., 2004; Newman & Kosson, 1986) and impairment in aversive conditioning (Flor, Birbaumer, Hermann, Ziegler, & Patrick, 2002).

Many of the findings supporting a 'hot' and 'cold' distinction have been replicated with regards to child and adolescent CU traits, providing evidence that youth with conduct problems and CU traits show a distinct emotional, cognitive and physiological profile compared to children with conduct problems without CU traits. For instance, studies have demonstrated reduced emotional responsivity as indexed by slower reaction times to negative emotional stimuli in children with conduct problems and CU traits compared to children with conduct problems without CU traits (Kimonis, Frick, Munoz, & Aucoin, 2007; Loney, Frick, Clements, Ellis, & Kerlin, 2003; Frick et al., 2003). Emotion recognition deficits, specifically fear, have also been demonstrated in studies comparing antisocial children high and low on CU traits (Dadds, Jambrak, Pasalich, Hawes, & Brennan, 2011; Blair, Budhani, Colledge, & Scott, 2005; Leist & Dadds, 2009) and in studies of community samples examining associations between CU traits and emotion recognition deficits (Blair & Coles, 2000; Dadds et al., 2006; Dadds, El Masry, Wimalaweera, & Guastella, 2008; Munoz, 2009). A link between CU traits and fearlessness or a behaviourally uninhibited temperament (after controlling for conduct problems) has also been demonstrated (Frick et al., 2003; Waller et al., 2016). Studies of physiological factors have demonstrated associations with reduced autonomic arousal, including reduced skin conductance response in antisocial samples (Kimonis et al., 2008; Munoz, Frick, Kimonis, & Aucoin, 2008a, 2008b) and reduced heart rate reactivity (Anastassiou-

Hadjicharalambous & Warden, 2008) in children with conduct problems and CU traits compared to children with conduct problems alone. Although neuorimaging studies in youth are limited, studies with antisocial and community samples have demonstrated associations between reduced amygdala responsiveness and CU traits consistent with the adult work (Marsh et al., 2008; Jones, Laurens, Herba, Barker & Viding, 2009; Sebastian et al., 2012; Viding et al., 2012). Further, and also consistent with the adult work, associations between CU traits and a reward dominant response style, passive avoidance learning and reduced sensitivity to punishment have been demonstrated (Frick et al., 2003, Munoz & Modecki, 2013; Vitale et al., 2005). Finally, children with conduct problems with CU traits have also been found to show other distinct cognitive correlates, including impairment in moral reasoning (Fisher & Blair, 1998) compared to children with conduct problems without CU traits. In the following section, the three key theoretical models in the literature regarding the development of CU traits will be outlined.

### *1.4 The development of CU traits*

One of the most influential theoretical conceptualisations of the development of psychopathy and CU traits draws upon the evidence from behavioural genetics studies, which suggest high heritability (Fontaine, Rijsdijk, McRory, & Viding, 2010; Larsson, Andershed, & Lichtenstein, 2006; Taylor, Loney, Bobadilla, Iacono & McGue, 2003) together with findings from neuroimaging studies and experimental work suggestive of neurocognitive deficits. Blair's theory (2006; 2007; 2013), originally referred to as a the 'Violence Inhibition Mechanism' and now as the 'Integrated Emotions Systems' (IES) theory emphasises that the key component to psychopathy (and CU traits) is an emotional deficit and places genetically based amygdala dysfunction at the root of this deficit. The amygdala is important in processing emotions, particularly fear, and is critical for stimulus-reinforcement learning, both of which are impaired in psychopathy and CU traits. According to the IES model, in normal development transgressions against others come to be regarded as "bad" because of the association of these transgressions with the aversive feedback of the distress from the victims. Amygdala dysfunction, and the consequent impaired stimulus-reinforcement learning and responsiveness to the distress of others, results in a deficient response to transgressions against others. Thus the

hypothesised amygdala impairment in children and adults with psychopathy and CU traits impairs their ability to learn not to harm others. IES theory has largely been based on findings from research with adults with psychopathy, adults with brain damage and animal work, but also on some findings from youth with CU traits and psychopathy (Herpers et al., 2014).

Another key theory regarding the development of psychopathy and CU traits provides an account of how the child's biologically based characteristics might reduce their learning about the outcomes of harmful behaviour, but places the emphasis on a fearless temperament. Frick and colleagues (Frick & Morris, 2004; Frick & White, 2008; Frick & Viding, 2009; Frick, Ray, Thornton, & Kahn, 2014) have drawn on work from developmental psychology by Kochanksa on the development of conscience to provide this account of the development of CU traits. In a serious of studies, Kochanksa and colleagues (Kochanska, 1995; Kochanska, 1997a; Kochanska, Askan, & Joy, 2007) have shown that 'fearless' children are unresponsive to parental discipline. Instead, parenting which capitalises on positive emotions has been found to particularly beneficial for the conscience development of fearless children. 'Conscience' is defined by the two key moral emotions of empathy and guilt, which are the key impairments in CU traits (Frick et al., 2014). Kochanksa (1993) proposes that the anxious arousal which follows transgressions and punishment is integral in the development of an internal system that functions to inhibit misbehaviour. Children with a fearless or behaviourally uninhibited temperament are thought to be less likely to experience this anxious arousal which puts them at risk for problems in conscience development. Historical accounts of psychopathy (Lykken, 1997) had also placed an emphasis on fearlessness in the development of psychopathy. Together this has given rise to the 'fearlessness' pathways to CU traits.

A third theoretical model places emphasis on the reduced eye contact shown by children with CU traits (Dadds et al., 2011). Dadds and colleagues have demonstrated that the facial fear recognition impairment found in children with conduct problems and CU traits can be ameliorated if the child is directed to look to the eyes (Dadds et al., 2006; Dadds et al., 2008). Dadds also places the amygdala as central to this theoretical model, drawing on findings from amygdala lesioned

patients who show a similar improvement in fear recognition after being directed to attend to the eyes (Adolphs et al., 2005). Dadds highlights how amygdala function is involved in the regulation of attention to, as well as responsiveness to, emotional and particularly fear stimuli. It is also involved in the detection and direction of eye gaze (Fox & Damjanovic, 2006). Eye contact is thought to be critical in understanding the emotional state of another person, and eye contact deficits have been proposed to underlie disorders of social cognition (Skuse, 2003). Dadds proposes that this failure to orientate to emotional stimuli causes children to miss vital communication, particularly from attachment figures in early development, and leads to a series of cascading errors in the development of empathy and conscience. In samples of children aged 4-8 years Dadds and colleagues (Dadds et al., 2012; Dadds et al., 2014) have demonstrated that children with conduct problems and CU traits show less eye contact with attachment figures during an observation assessment where mothers are asked to express love to the child.

### *1.5 The parenting environment and CU traits*

In this section, the role of the parenting environment in the development of CU traits will be discussed. All three key theoretical models reviewed in section 1.4 allow for the influence of the parenting environment on the development of CU traits, or conduct problems in the presence of CU traits, to varying degrees. The IES model proposes that children are at a significant disadvantage to be able to benefit from parenting due to the impairment in stimulus-reinforcement association formation. However, the broader family environment can still play a role in the transmission of antisocial behaviour from parents to children, as without empathic responsiveness the child is more susceptible to learning antisocial strategies from their environment (Blair, 2006). In Dadds theory regarding a failure to orientate to emotional stimuli, the child is still able to benefit from parental input, they are just deprived of a substantial amount of parental communication from reduced attention to the eyes of parents. Dadds has proposed orienting the child to the eyes of attachment figures as a potential treatment target for children with CU traits (Dadds et al., 2012; Dadds et al., 2014). Finally, the application of Kochanska's work on conscience development (fearlessness theory; Frick & Viding, 2009) suggest that

children with CU traits are less likely to be influenced by parental discipline due to lack of anxious arousal, but that they may benefit from warm and positive parenting practices, which do not require anxious arousal to internalise and have been shown to promote conscience development in fearless children.

Parenting practices, in particular, harsh and inconsistent parenting, have been consistently linked to the development of conduct problems (Gershoff, 2002; Patterson, 2002). As reviewed in section 1.3, there are numerous findings supporting a biological basis for CU traits. Further, behavioural genetics studies have also demonstrated that conduct problems with CU traits appear to be more highly heritable than conduct problems without CU traits (Viding et al., 2008) and CU traits alone have also been found to show moderate to high heritability (Fontaine et al., 2010; Larsson et al., 2006; Taylor et al., 2003). Further, many studies have shown that typical conduct problem interventions are less effective for children with accompanying CU traits (Caldwell, McCormick, Wolfe, & Umstead, 2012; Dadds, Cauchi, Wimalaweera, Hawes, & Brennan, 2012; Haas et al., 2011; Hawes & Dadds, 2005; Kolko & Pardini, 2010; Masi et al., 2013; Waschbusch, Carrey, Willoughby, King, & Andrade, 2007) although most studies do not account for the higher conduct problem severity in children with CU traits (Hyde, Waller, & Burt, 2014). This has led some to conclude that CU traits, and conduct problems accompanied by CU traits, are less susceptible to environmental influence. Initial studies examining the role of the parenting environment tested whether CU traits moderated the association between parenting, particularly harsh parenting, and conduct problems. They concluded that children with conduct problems and CU traits are less responsive to parenting (e.g. Oxford, Cavell, & Hughes, 2003; Wootton, Frick, Shelton & Silverthorne, 1997). However, this conclusion may be somewhat premature as over the past 10 years there has been increasing interest in, and recognition of, the role of varying aspects of parenting in the development of CU traits, not necessarily yet targeted in standard social-learning theory-based interventions.

Studies examining parenting and CU traits have taken two approaches. The first approach is designed to address the question of whether CU traits moderate the influence of parenting on child antisocial behaviour. The second has examined the direct prediction from parenting to child CU traits. Each approach will be considered

in turn. Research findings examining the moderating role of CU traits in the association between parenting and antisocial behaviour have largely been consistent with Kochanska's findings on conscience development. The early and frequently cited studies examining this question relied on parent report of parenting and used cross-sectional designs (Whooten et al., 1997; Oxford et al., 2002; Hipwell et al., 2007) and they broadly provided support for the proposal that the conduct problems of children with CU traits is less influenced by harsh parenting. Some recent studies have employed observed measurement and longitudinal designs. For example, Pasalich, Dadds, Hawes, and Brennan (2011) studied 95 boys aged 4-12 years with conduct disorder or ODD diagnosis. They assessed maternal and paternal warmth, based on affective attitudes expressed about the child during a Five Minute Speech Sample (FMSS). Harsh parenting was assessed as coercion (coded from a family interaction task). Similar to Whooton et al. and Oxford et al., Pasalich et al. found an interaction with harsh parenting, such that children with CU traits showed higher conduct problems regardless of their experience of parental coercion. However, they also found an interaction for maternal and paternal warmth. They found that children with high levels of CU traits showed decreased conduct problems in the presence of warmth, whereas warmth was not associated with conduct problems in children with low levels of CU traits. Kochanksa, Kim, Boldt, and Yoon (2013) replicated this finding with a community sample of 100 children followed longitudinally for 5 years. They coded observed mother-child and father-child shared positive affect and 'mutually-responsive orientation' (MOI), defined as a close, warm, and mutually cooperative relationship between the parent and child (Kochanska, 1997b) at age 3-4 years and examined interactions with CU traits measured at age 5.5 years as predictors of externalizing problems at age 6.5 to 8 years. Significant interactions were found for father-child shared positive affect and mother-child MOI. In both instances, positive parenting predicted decreased externalizing behaviour at high but not at low levels of CU traits, after controlling for early externalizing behaviour. This interaction has now been further replicated; once in a sample of 364 children at risk for behaviour problems followed longitudinally from 3-4 years, using the same measure of warmth as Pasalich et al. and an observed coding of 'positive behaviour support' (Waller et al., 2015) and once using questionnaire report of warmth in a sample of 1233 7-8 year old low-income girls followed longitudinally for 4 years (Kroneman, Hipwell, Loeber, Koot, & Pardini, 2011). Collectively these findings

support a role for parental warmth and other aspects of 'positive' parenting in the reduction of conduct problems in children with CU traits. The findings also support the contention that conduct problems accompanied by CU traits as less influenced by negative parenting practices.

A number of studies designed to examine the direct prediction from parenting to CU traits have found both harsh and more 'positive' parenting to significantly predict CU traits with some reports that prediction from parenting environment may vary in girls and boys. Studies have also varied in their reliance on maternal reports of parenting or in their use of observational methods to assess quality of parenting. Each approach to the assessment of parenting will be considered in turn.

Pardini, Lochman, and Powell (2007) examined the prediction from parent report of parenting, assessed using the Alabama Parenting Questionnaire (APQ; Frick, 1991), and child report of parental warmth/involvement, to CU traits in a sample of age 10-11 year old children over-sampled for aggression and followed longitudinally for one year. Lower child-reported parental warmth and higher parent-reported physical punishment predicted increased mother and teacher reported CU traits, after accounting for time 1 CU traits and antisocial behaviour. Hawes, Dadds, Frost, and Hasking (2011) also used the APQ with a population-based sample of 1008 children (52.6% boys) aged between 3 and 10 years. Of the five dimensions assessed by the APQ only low positive reinforcement significantly predicted CU traits over the period of one year, after accounting for antisocial behaviour and other covariates. The authors did also report a significant interaction with sex, with the association being much stronger in girls than boys. Parental involvement predicted decreased levels of CU traits only in interaction with sex, with post hoc probing indicating this was stronger in boys. Parental use of physical punishment did not predict CU traits, unlike Pardini et al. Similarly, Barker et al. (2011) examined prediction from mother report of warmth and harshness at age 3 and 4 in a SEM analysis with prenatal risks and fearless temperament to CU traits at age 13 and examined processes separately in girls and boys. They reported small significant predictions from lower maternal warmth in girls and higher maternal harshness in boys to increased child CU traits, in a model which also accounted for the association between CU traits and conduct problems.

A series of studies reported by Waller and colleagues have examined prediction from observational as well as parent report of warm, positive, parenting to CU traits in early childhood. In these studies the authors created a hybrid measure of CU traits from other child problem behaviour scales (Hyde et al., 2013) and they labelled the construct 'deceitful callous (DC) behaviours' since two of the five items sampled referenced deceitfulness or manipulativeness. This measure is described more fully in Chapter 3 of this thesis. Waller et al. (2012) examined 'positive behaviour support' as their index of parenting, coded from mother-child interactions; this composite comprised a number of codes assessing verbal and physical support for the child's positive behaviour, with a focus on the parent structuring child behaviour. Parental harshness was also assessed from parental report and coded from the interactions. They examined prediction from parenting at age 2 years to CU traits at age 3 and 4 years, after accounting for earlier CU traits measured at age 2, and found only harshness (both observed and parent-report) predicted an increase in CU behaviours. In a further analysis on the same sample, Waller et al. (2014) used 'positive behaviour support' and also parental warmth coded from the FMSS at age 2 and 3 years. Waller and colleagues examined bidirectional effects between CU traits, parenting and behaviour problems in cross-lagged models. They found both FMSS warmth and positive behaviour support to predict decreased CU traits, after accounting for earlier CU and earlier and concurrent behaviour problems. They also found CU traits to predict decreased positive parenting over time. A key issue with studies of parenting and child CU traits is the possibility of passive and evocative gene–environment correlations, whereby parents who are more sensitive and warm have children with lower CU behaviours. Waller et al. (2017) attempted to rule out this possibility by examining associations between parenting and CU traits in an adopted sample (n = 261). Positive behaviour support was coded at age 27 months, and an ASEBA based CU measure was created based on work by Willoughby, Waschbusch, Moore, and Propper (2011). They found small significant associations between low positive behaviour support and CU traits for both primary and secondary caregivers.

A smaller number of investigations have examined parenting much earlier in infancy as a predictor of later child CU traits. There is evidence that infants as young

as 5 weeks (Bedford, Pickles, Sharp, Wright, & Hill, 2014) and six months of age (Wagner et al., 2016) show behaviours associated with later CU traits, which suggests that elements of early-mother infant interaction may have a key role to play in increasing or decreasing child CU traits. All of these studies to date have examined the role of maternal sensitivity. Maternal sensitivity refers to the quality with which mothers respond to their infants' cues in a timely and appropriate manner. Sensitive mothers respond to the child's gestures, expressions and communications reasonably quickly, with responses that are well matched to their infants' cues, the developmental level of their infant, and the demands of the current situation (Leerkes, Blankson, & O'Brien, 2009). Mother's responsiveness has been key to Kochanska's theorising regarding the optimal parenting for children who experience low anxious arousal. Further, findings from longitudinal studies of child empathy development have indicated that maternal sensitivity in infancy predicts increased empathic responding in early childhood (Kochanska, Forman, & Coy, 1999; Spinrad & Stifter, 2006).

In a previous publication from the Wirral Child Health and Development Study sample used in this thesis, general maternal sensitivity assessed at seven months in a play-based interaction and coded using the National Institute of Child Health and Development (NICHD) sensitivity coding (Owen, 1992) predicted CU traits at age 2.5 years, in girls only (Bedford et al., 2014). In a study covering a much longer timespan, Centifanti, Meins, and Fernyhough (2016) found that mind-mindedness, indexing the mother's awareness of her infant's states of mind, assessed at age 8 months predicted children's self-report of CU traits at 10 years. However, in this study, maternal sensitivity, despite being associated with mind-mindedness, did not predict CU traits. In another study, Wagner et al. (2016) coded maternal sensitivity using the NICHD coding at 6 months during the still face procedure on a sample of 206 children. They combined sensitivity into a composite with five other codes and demonstrated a small weak negative association with CU traits measured from age 2-4 years.

In sum, while there is evidence that the conduct problems in children with CU traits is less responsive to harsh parenting than the conduct problems of children without CU traits, findings from studies examining the development of CU traits

suggests that harsh parenting drives increases in CU traits. However, the key findings to come from both approaches to analysis of parenting and CU traits are those which implicate the importance of more 'positive' aspects of parenting for driving decreases in child CU traits, and decreases in conduct problems in the presence of CU traits. A range of different positive parenting characteristics have been implicated, with some measures focusing on maternal sensitivity early in infancy and some focussing on active praise-based structuring of behaviour such as observed positive behaviour support and positive reinforcement assessed by the APQ. Other measures, such as the FMSS and APQ positive involvement scale, index the parent's feelings/attitudes towards the child and the quality of the parent-child relationship. Of course all measures of 'positive' parenting assess 'warmth' to varying degrees. In order to accurately inform the targets of parenting interventions it is of critical importance to identify which specific components of 'positive' parenting are associated with reductions in CU traits. Are expressions of warmth and love all that is needed? Or do other more active parenting elements such as positive reinforcement or sensitive responsiveness also serve an important role and under what conditions? In pursuit of this question a recent development in the literature has been to examine aspects of parental sensitivity a little more closely. These studies are reviewed next.

### *1.6 Parental sensitivity to distress*

In studies of the role of early mother-infant interactions in the development of attachment security, a distinction has been made between sensitivity to distress and to non-distress on the grounds that a parent's ability to help an infant regulate distress is likely to be key to the development of emotion regulatory capacities seen in the Strange Situation Procedure (Goldberg, Grusec, & Jenkins, 1999; McElwain & Booth-Laforce, 2006; Thompson, 1997). Evidence in support of this hypothesis has been reported (Leerkes, 2011; McElwain & Booth-Laforce, 2006). This distinction may also be relevant to the origins of CU traits because CU traits are conceptualised as a deficit in affective empathy (Jones, Happe, Gilbert, Burnett, & Viding, 2010). Furthermore, CU traits are characterised by impaired responsiveness to distress in others so it seems likely that a parenting environment where the child's own distress emotions are sensitively responded to may help foster the child's ability to respond to

the emotions of others. It is possible that the early experience of parental sensitivity specifically in response to distress, promotes empathy via processes such as modelling (Kiang, Moreno, & Robinson, 2004) or imitation (Baird, Scheffer, & Wilson, 2011). Davidov and Grusec (2006) have previously argued for a specific link between responsiveness to distress and child empathy. They tested this hypothesis in a sample 6-8 year olds examined in cross-section. When considered simultaneously, sensitivity to distress, but not warmth, was associated with increased child empathy. Further, an evaluation of the mechanisms of change in a randomized controlled trial (RCT) of the effect of foster care in children experiencing early institutional deprivation showed that observed sensitivity to distress, and not warmth, assessed at 2-3 years, predicted lower CU traits in early adolescence (Humphreys et al., 2015).

Thus there is reason to suppose that sensitivity to distress would be a stronger predictor of reduced child CU traits than parental warmth. In some approaches to studying general sensitivity in the literature, parental warmth has been included as part of the sensitivity construct (e.g. NICHD Early Child Care Research Network, 1997; Wagner et al., 2016) which makes it difficult to reach conclusions about the specific roles of warmth and sensitivity. In Chapter 4 of this thesis the contribution of maternal sensitivity to distress and maternal positive regard (warmth) as well as sensitivity to non-distress and intrusiveness (as an infant relevant index of harshness) to child CU traits measured over the period 2.5 to 5 years is examined.

Maternal sensitivity, and maternal sensitivity to distress, is associated with infant attachment security (McElwain & Booth-LaForce, 2006; Leerkes et al., 2011; Wolff & Ijzendoorn, 1997). Three studies have implicated a role for attachment in the development of CU traits. Evidence for an association between attachment status and child CU traits comes from a study of 3–9 year olds referred with conduct problems (Pasalich et al., 2012). Higher CU traits were associated with insecure and with disorganized attachment, based on the Manchester Child Attachment Story Task (Green, Stanley, Smith, & Goldwyn, 2000). Willoughby, Mills-Koonce, Gottfredson, and Wagner (2014) showed that attachment disorganization assessed at 3 years was associated with a stronger association between the combination of ODD and CU traits and aggression, although they did not examine its association with CU traits in multivariate analysis. A recent study provided evidence that attachment related

processes may mediate the association between parental sensitivity and CU traits. Wagner et al. (2015) found that the association between low parental sensitivity and CU traits was mediated in part by scores for dysfunctional family representations derived from children's drawings of their families completed in first grade. Thus empathy, and hence lower CU traits, may be promoted by internalization of the experience of empathic responding by parents. In light of this evidence, Chapter 4 also examines whether any associations found between parenting and child CU traits are mediated by child attachment status.

### *1.7 Early childhood CU traits*

The above review has covered findings from studies of CU traits from age 2 to 18 years. However, the application of the construct of CU traits to toddler and preschool age children is a relatively recent development and there is still some doubt that CU traits can be measured at this early age. On the other hand there is reason to believe that meaningful variations in CU traits may be identifiable by age two years. Observational studies have identified that empathy-related behaviours and guilt emerge during the first and second years of life (Kochanska, Gross, Lin & Nicholas, 2002; Vaish, Carpenter, & Tomasello, 2009). Furthermore, trajectories of elevated aggressive behaviour have also been demonstrated to start in the second year of life (Tremblay et al., 2004; Campbell, Spieker, Burchinal, & Poe, 2006) and if CU traits play a causal role in the development of persistent aggressive behaviour, then CU traits or their precursors may be measurable and operating at this early age too. Chapter 3 reviews the existing studies on CU traits in children under five years of age in detail so this will not be repeated here. However, a meta-analysis, not included in the introduction to that paper, has now been published reviewing studies reporting on the association between CU traits measured under the age of five years and conduct problem severity (Longman, Hawes, & Kohlhoff, 2016). The meta-analysis found a moderate effect size for the association ($r = .39$, $p<.001$) from 10 studies comprising $n = 5731$ participants, supporting the utility of the measurement of CU traits prior to school-entry.

There would be significant potential benefits to being able to measure CU traits in young children. The ability to implement intervention before serious conduct problems become established would be a clear benefit, with evidence suggesting that interventions for serious antisocial behaviour later in childhood are much less effective than interventions employed earlier (Rutter, Giller & Hagell, 1998). Research investigations addressing the developmental pathways to CU traits, which are crucial for informing intervention, would also benefit from early measurement. However, it is critical that researchers are mindful of the potential stigmatising effects of labelling a young child as 'callous and unemotional'. The use of the terminology 'trait' also implies that CU traits are more stable than other child problems dimensions. There is also a greater concern with younger samples that behaviours actually reflecting developmental delay or developmental disorders such as autism will be identified as CU traits (Waller et al., 2017). For these reasons, Hyde, Waller and colleagues (Hyde et al., 2013) have advanced the use of the term 'CU behaviours' when considering CU traits in young children. This terminology is also better suited to the nature of assessment of CU traits in young children, which relies almost exclusively on parent report of observable behaviours. Whilst mindful of this distinction, in this thesis the terminology CU traits has been used throughout for consistency.

Another key concern when measuring CU traits in young children is the use of measures developed with adolescents and older children which often contain items that when applied to a toddler or preschool aged child will likely reflect developmental immaturity rather than CU traits. To combat this, researchers' have created hybrid measures from existing child problem behaviour measures, although these measures often lack items assessing the core feature of CU traits, for instance, lack of empathy. Chapter 3 evaluates the psychometric properties of a hybrid measure created from supplementing an established CU traits measure with items from early child problem behaviour measures.

### *1.8 CU traits and violent and aggressive behaviour*

The most important function of the construct of psychopathy in adults is that it identifies a subgroup of antisocial individuals who show more severe and persistent violent behaviour (Leistico, Salekin, DeCoster, & Rogers, 2008; Douglas, Vincent, & Edens, 2006; Porter & Woodworth, 2006). While non-violent forms of antisocial behaviour have potential to prove more costly to society, violence is the most damaging in terms of the physical and psychological consequences for the victims and the psychological impact on the wider social network around victims. In this section, studies examining associations between CU traits or psychopathy and physical aggression or violence in children and adolescents will be reviewed. Studies of psychopathy in adolescents have replicated the link between psychopathy and severe violence found in adults, with psychopathy associated with committing sexual (Caputo, Frick, & Brodsky, 1999) and violent (Murrie, Cornell, Kaplan, McConville, & Levy-Ekon, 2004) offences, as well as increased violent recidivism (Brandt, Kennedy, Patrick & Cutrain, 1997; Gretton, Catchpole, & Hare, 2001). Within adolescent offender samples, psychopathy has been associated with a range of violent outcomes, including use of excessive violence during violent crime (Lindberg et al., 2009), use of a weapon (Kosson, Lorenz, & Newman, 2006; Murrie et al., 2004), use of multiple weapons (Kosson et al., 2006) and inflicting injury on victims (Murrie et al., 2004). CU traits specifically have been associated with a history of violence against females, multiple violent incidents against the same person, unprovoked violence and a history of weapon use in male adolescent offenders (Kruh, Frick, & Clements, 2005). CU traits in children have been linked to aggressive behaviour, in particular studies have shown that CU traits are more strongly linked to proactive aggression than reactive aggression (Frick et al., 2003; Fanti, Frick & Georgiou, 2009; Marsee & Frick, 2007).

The best test of the utility of the construct of psychopathy and CU traits is arguably whether they show prediction to violence after accounting for broader indices of antisocial behaviours; this has been referred to as incremental validity (Kruh et al., 2005). Evidence for incremental validity has been demonstrated for psychopathy in adolescents. For example, psychopathy has been shown to predict number of violent offences (Salekin, Neumann, DiCicco, & Duros, 2004) after controlling for conduct problems, age of onset of criminal behaviour and criminal versatility, and predict severity of injury to the victim (Vitacco, Caldwell, Van

Rybroek, & Gabel, 2007) after controlling for conduct problems, oppositional defiant disorder and ADHD, in offender samples. Murrie et al. (2004) found psychopathy scores to predict instances of institutional violence after controlling for past violent behaviour in a sample of incarcerated adolescents. Gretton et al. (2004) conducted a 10 year follow up on a sample of 12-18 year olds who were court referred for forensic assessment and found that psychopathy scores from adolescence predicted violent recidivism in adulthood, after controlling for initial conduct disorder, age at first offence, and past history of violent and nonviolent offending. A number of studies have also provided evidence for the incremental validity of CU traits in predicting violent and aggressive outcomes. After controlling for history of antisocial behaviour, Lawing, Frick, and Cruise (2010) found CU traits to predict number of sexual offence victims, greater planning of sexual offences and greater violence against the victim in adolescent sex offenders. Kruh et al. (2005) found CU traits to predict frequency and variety of violent crimes, after controlling for past criminal behaviour and risk for recidivism scores, in a sample of adolescent offenders. Two studies over a somewhat younger age range have also supported the incremental validity of CU traits in predicting aggression. In a general population sample of 9-14 year olds CU traits were associated with physical aggression, after accounting for conduct disorder symptoms (Thornton, Frick, Cranpanzano, & Terranova, 2012), and in a study of boys aged 9-13 over-sampled for conduct problems, CU traits predicted self-reported violent behaviour over a 2 year follow up, after accounting for conduct problems, ODD symptoms and ADHD symptoms (Pardini & Fite, 2010). Chapter 3 assesses the incremental validity of the early childhood CU measure to prospectively predict aggressive behaviour after accounting for initial aggression.

### *1.9 How do CU traits translate to aggressive behaviour?*

As described in section 1.8, CU traits are associated with violent and aggressive behaviour. However, this association is typically modest in size, highlighting that not all children with CU traits are aggressive. The issue of how an indifference to others distress (i.e. CU traits) is translated into aggressive behaviour is an important yet largely unexplored question. Why, and how, does a lack of empathy, guilt and concern for others cause one to want to hurt other people, as opposed to simply rendering one indifferent to others? Since not all children with CU

traits show aggressive behaviour, there must be additional processes involved in the translation of CU traits to aggression. The theoretical models regarding CU traits outlined in section 1.4 offer an explanation as to why individuals with CU traits lack inhibition for antisocial behaviour, suggesting this is either due to unresponsiveness to distress emotions in others, reduced ability to learn from socialisation or lack of anxious arousal associated with transgressions, but they do not offer a full account as to why some individuals with CU traits do not show aggressive behaviour. Investigations explicitly designed to test this question are rare. In this section, the relevant literature is reviewed and a candidate biological moderator of the association between CU traits and aggression is proposed.

Very few studies have examined moderators of the association between CU traits and aggression. As highlighted in section 1.4 Blair (2006) proposes that a deficit in empathic responsiveness facilitates the learning of antisocial strategies from the environment. Consistent with this proposal, a large-scale study with a nationally representative sample of 13-18 year olds found that low neighbourhood income (an index of neighbourhood antisociality) moderated the association between CU traits and violent delinquency (Markowitz, Ryan, & Marsh, 2015). In another study of a community sample of adolescents (mean age 16), deficits in reflective functioning were found to moderate the association between psychopathic traits and proactive aggression (Taubner, White, Zimmerman, Fonagy, & Nolte, 2013). Other studies have been designed to examine mediators of the association between CU traits and aggression (e.g. Howard, Kimonis, Munoz, & Frick, 2012) but such a design is not suited to examining why some individuals with CU traits develop aggressive behaviours and others do not.

Tremblay (Tremblay, 2000; Tremblay & Nagin, 2004) has provided a persuasive account of the origins of aggressive behaviour from a thorough review of the literature over the past century and drawing on more recent work examining trajectories of physical aggression throughout childhood. His account is largely based on two forms of evidence. Firstly, that children show aggression from the second year of life (Tremblay et al., 1999; Hay, Castle, & Davies, 2000) generally over competition for resources (Hay, 2005). Secondly, trajectory studies have repeatedly shown that while aggression increases from infancy and peaks at preschool age, after

this point physical aggression decreases throughout childhood, adolescence and into adulthood (Broidy et al., 2003; Cote, Valliancourt, LeBlanc, Nagin, & Tremblay, 2006; Lacourse et al., 2002; Tremblay et al., 2004; White, Bates, & Buyske, 2001). Such a pattern could not be explained by social learning theories which propose that children learn to use aggression from their environment. Rather, Tremblay argues that humans are born genetically programmed to use physical aggression, and throughout childhood we learn *not* to aggress. This learning to control process was labelled socialization, and he proposed that individual differences in both contextual and individual factors explain why some children do not learn to control or inhibit aggression. Within this framework, reduced physiological reactivity could be a plausible mechanism through which failures in inhibition of aggression might occur, and more so in the presence of CU traits which create an indifference to others' suffering. Chapter 5 of this thesis examines the potential moderating role of cortisol reactivity in the association between CU traits and aggression. The rationale for examining this as a potential moderator is detailed in that chapter but a broader background context is given below.

As reviewed in section 1.3, CU traits have been associated with reduced physiological arousal in a number of studies. Low physiological arousal is thought to be a biological marker for low fear, consistent with the proposed fearlessness pathway to CU traits. Although there are still relatively few studies in childhood, reduced autonomic reactivity assessed via heart rate (Anastassiou-Hadjicharalambous & Warden, 2008) and skin conductance (Kimonis et al., 2008; Munoz, Frick, Kimonis, & Aucoin, 2008a, 2008b) have both been reported. Some studies have also reported associations with HPA-axis activity, by demonstrating group differences or associations with the stress hormone cortisol. In a sample of clinic-referred boys (Burke, Loeber, & Lahey, 2007), as well as in a male community sample (Loney, Butler, Lima, Counts, & Eckel, 2006), groups with high CU traits exhibited significantly lower basal cortisol levels than did low CU traits groups. In females, differences were nonsignificant (Loney et al., 2006). However, another study found no association between basal cortisol and CU traits in adolescents (Poutska et al., 2010). There is evidence that basal cortisol and cortisol reactivity to a stressor reflect different mechanisms (Herman et al., 2016). When considering the translation of CU traits to aggressive behaviour, cortisol reactivity would seem to be more relevant, as

aggression typically occurs in stressful situations where the HPA-axis is activated. One study examined associations between CU traits and cortisol reactivity to a social stressor. In a sample of adolescents with ADHD, Stadler et al.,(2011) demonstrated a significant negative association between cortisol reactivity and CU traits. Theoretical accounts as to why reduced HPA-axis activity may lead to antisocial behaviour include sensation seeking theory (Zuckerman, 1979) and fearlessness theory (Raine, 1986).

Sensation seeking theory proposes that people who are characterized by low autonomic arousal experience this as an aversive state and are therefore predisposed to seek stimulation, for example, by fighting, to increase their low levels of arousal. Fearlessness theory, which has since been proposed to underlie the development of antisocial behaviour with CU traits as reviewed in section 1.4, proposes that low physiological arousal is a marker for low fear, and low fear permits the execution of aggression towards others as the individual does not fear the consequences of their actions and low fear also reduces the effectiveness of socialisation. Chapter 5 provides an overview of the literature on reduced HPA-axis activity and antisocial behaviour in children. However in brief, the evidence has been inconsistent. In a meta-analysis in 2008 no overall association between cortisol reactivity and broad externalising problems was found, with some significant associations found for basal cortisol (Alink et al., 2008). The evidence also suggests that there may be important sex differences in the risk from physiological arousal, with reduced arousal posing the risk for males and increased reactivity posing the risk for females (e.g, Dietrich et al., 2013; Sandman, Glyn, & Davis, 2013; Tibu et al., 2014). In Chapter 5, the case is made for examining the hypothesis that the combination of the emotional responsiveness impairment characteristic of CU traits in combination with reduced HPA-axis reactivity may create an elevated risk for aggressive behaviour. It is also proposed that this may be a male specific mechanism.

### *1.10 Sex differences in antisocial behaviour, aggressive behaviour and CU traits*

Conduct problems and antisocial behaviour are more prevalent in males and so understandably the majority of studies of antisocial behaviour and CU traits have focused on male only samples. Sex differences in rates of aggressive behaviour (Baillargeon et al., 2007; Card, Stucky, Sawalani & Little, 2008) and antisocial behaviour (Offord, Alder, & Boyle, 1986; Moffit, 2001) have been documented throughout the lifespan and beginning in the second year of life (Baillargeon et al., 2007). Boys are more likely than girls to belong to elevated trajectories of aggression (Cote et al., 2006; Tremblay et al., 2004) and physical aggression declines with age more in girls than in boys (Lee, Baillargeon, Vermunt & Tremblay, 2007). Similarly, boys show higher rates of CU traits than girls (Ezpeleta, Osa, Granero, Penelo, & Domenech, 2013; Fanti & Kimonis, 2013; Marsee, Silverthorne & Frick, 2005) and the same has been found for adults in relation to psychopathy (Cale & Lilienfeld, 2002).

Historically violence and antisocial behaviour have been considered a male phenomenon. However, adult female and particularly juvenile female arrests and prosecutions are increasing (Holmes, 2010) and there is growing recognition of the need to study antisocial behaviour in females. There is some evidence that females show differences in aggressive behaviour, for example, findings from adults have indicated that females are more likely than males to show aggression towards family, friends and acquaintances than strangers (Robbins, Monahan, & Silver, 2003). Females are just as likely as men to perpetrate relationship abuse (Archer, 2000; Dutton & Nicholls, 2005; Nicholls & Dutton, 2001; Straus, 1999) and are the most frequent perpetrators of child abuse (Dutton, 2006). There is some evidence that girls and adolescent females use relational and indirect aggression more than males (Crick & Grotpeter, 1995; Stickle, Marini, & Thomas, 2011 but see Marsee, et al., 2005). Some evidence also suggests that young girls are better able to hide their aggressive behaviour then boys (Pepler & Craig, 1995). Aggressive behaviour in females may show different consequences; aggressive females are more likely to be rejected by their peer groups (Pepler, Craig, Ziegler, & Charach, 1993) and as females are typically responsible for the majority of parenting of the next generation, associated parenting impairments and social care or child welfare involvement (Chamberlain & Moore, 2002 Robins, 1986; Serbin, Peters, McAffer, & Schwartzman, 1991) may contribute to the transmission of antisocial behaviour to the next generation.

Loeber and colleagues (Loeber & Keenan, 1994) have proposed that conduct disorder is characterised by a gender paradox, where despite the fact that males show a higher prevalence of conduct disorder diagnosis, females who do meet threshold for diagnosis actually show more severe behavioural problems. This has been observed in clinical samples of children with conduct disorder (Eme, 1992; Webster-Stratton, 1996) and in psychiatric adult samples (Nicholls, Ogloff, & Douglas, 2004) and is also supported by higher co-moborbidity in females, particularly with depression and anxiety (Keenan, Loeber, & Green, 1999), with evidence that comorbid internalising and externalising problems are associated with worse outcomes than single disorders (Dishion, 2000; Angold & Costello, 1993).

There are a number of explanations for this supposed gender paradox, including that current diagnostic criteria developed from males do not adequately 'fit' female antisocial behaviour (i.e. the expression of antisocial behaviour differs in females), that there may be a gender bias in the rating of antisocial behaviour, or that it may present and manifest similarly enough but females require different thresholds (i.e. the same level of antisocial behaviour in males and females represents higher severity in females) perhaps because females require more risks than males to display antisocial behaviour or because antisocial behaviour deviates further from expected gender-role behaviour in females. A consideration of typical biologically influenced gender traits and gender role expectations is rarely discussed in the literature but seems exceptionally relevant, especially in relation to CU traits.

Broadly, elements of antisocial behaviour, particularly aggression, are more accepted and encouraged in males than in females. When specifically considering CU traits, it is relevant that in normative development there is some evidence that girls show higher concern for others (Keenan & Shaw, 1997; Lennon & Eisenberg, 1983), more prosocial behaviour (Eisenberg & Fabes, 1998) and more guilt (Kochanska, Gross, Lin, & Nichols, 2002) than boys do. And although a fearlessness pathway to the development of CU traits and psychopathy has been advanced (Frick & Viding, 2009; Frick & Morris, 2004; Frick et al., 2014b), gender differences may be relevant since in normative development girls have been found to be more likely to be fearful than boys (Cote, Tremblay, Nagin, Zoccoilillo, & Vitaro, 2002)

although many studies do not find sex differences in child fearfulness (e.g. Kochanska, 1997). Thus a female and a male manifesting the same level of CU traits may not be the same, since the female has perhaps deviated more markedly from her expected gender role characteristics.

Studies on sex differences in CU traits has shown that, similar to findings from the broader phenotype of conduct problems and externalising problems, CU traits in girls but not boys are associated with internalizing problems (Essau, Sasagawa, & Frick, 2006). Further, girls are more likely to belong to clusters of psychopathic traits or CU traits with accompanying anxiety (so called "secondary psychopathy") than males (Euler et al., 2015; Meehan, Maughan, Cecil, & Barker, 2017) or be more likely to belong to this cluster than a "primary" cluster, without anxiety (Hicks, Vaidanathan, & Patrick, 2004; Vaughn, Edens, Howard, & Smith, 2009; Gill & Stickle, 2016).

Collectively, the literature reviewed indicates that consideration of sex differences in the study of CU traits and CU traits and conduct problems is of paramount importance. If CU traits present differently in males and females, it is essential to first establish that measures are invariant by sex. It must also be established that CU traits show the same utility in females at predicting antisocial behaviour as they do in males. In Chapter 3 of this thesis, we sought to establish that the measures used to assess CU traits were invariant by sex. We also tested for sex differences in associations between CU traits and aggression; as reviewed in section 1.9, sex differences are also key to the analysis in Chapter 5.

Evidence for measurement invariance by sex has been shown for the Inventory of Callous-Unemotional traits (ICU; Frick, 2004), which is currently the gold standard measure of CU traits in childhood, in community samples of 3 year olds (Ezpeleta et al., 2013), 11-13 year olds (Ciucci, Baroncelli, Franchi & Golmaryami, 2014) and 13-18 year olds (Essau et al., 2006). The Antisocial Process Screening Device (APSD; Frick & Hare, 2001), the precursor to the ICU, has also been shown to be sex invariant as an entire psychopathy measure in a sample of 9-10 year olds twins (Dong, Wu, & Waldman, 2014). Importantly, the limited number of studies of CU traits to date which have considered the role of sex differences in

associations with antisocial outcomes have provided evidence that whilst CU traits are lower in females, they appear to show the same utility in predicting antisocial outcomes as they do in males. Studies which examined interactions between CU traits and sex have found no moderation in prediction of offending (McMahon, Witkiewitz, & Kotler, 2010) future conduct problems (McMahon et al., 2010), bullying (Viding, Simmonds, Petrides, & Fredrickson, 2009 but see Thornton et al., 2012) and aggression (Thornton et al., 2012) in samples over the mid childhood to adolescence age range. Similarly, studies over this age range which have estimated associations separately by sex have found comparable associations between CU traits and aggression in boys and girls (Essau et al., 2006; Kimonis et al., 2006; Silverthorne, Frick, & Reynolds, 2001). With younger children, Dadds, Hawes, Frost, and Fraser (2005) reported that CU traits did not prospectively predict antisocial behaviour in 4-6 year old girls but did in 7-9 year old girls, when for boys prediction was found in both age groups. However, this antisocial behaviour outcome comprised the majority of the narcissism items from the APSD as well as the conduct problem items from the strengths and difficulties questionnaire so differs from antisocial behaviour outcomes used in other studies. Notably the other large scale studies of CU traits in early childhood, reviewed in Chapter 3, have not tested for sex differences in associations with outcomes.

### *1.11 Aims and outline of the present thesis*

The first aim of this thesis was to examine the psychometric properties and reliability of a hybrid measure of CU traits at age 2.5 years and test whether CU traits measured at this age show the same utility in predicting physically aggressive behaviour as that found for older children. The second aim was to examine the contribution of parenting in infancy to early childhood CU traits, and specifically to compare different specific components of parenting (warmth, sensitivity to distress, sensitivity to non-distress and intrusiveness) in this regard. This analysis also examined whether any associations found might be mediated by attachment status. The third aim was to investigate a possible mechanism through which CU traits may translate to aggressive behaviour. The moderating role of cortisol reactivity in the association between CU traits and aggression from age 5 to 7 years was examined,

with the prediction that, in boys only, reduced reactivity would increase the risk for aggression in the presence of CU traits.

This thesis comprises three empirical chapters. All chapters contain data collected as part of the same ongoing, longitudinal, prospective study investigating the earliest origins of childhood conduct problems; the Wirral Child Health and Development Study (WCHADS). Chapter 2 describes the WCHADS sampling procedure and recruitment and gives a brief overview of the assessment phases.

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# Chapter 2: Wirral Child Health and Development Study (WCHADS) method

In the section the initial recruitment to the study will be described with a brief overview of the assessment phases. The assessment phases relevant to this thesis will be highlighted.

## 2.1 WCHADS Ethics Statement

Ethical approval for phases 1 to 8 of data collection on the WCHADS was granted by the Cheshire North and West Research Ethics committee on the 27th June 2006 (reference number 05/Q1506/107). Ethical approval for phases 9, 10, 11 and 12 of data collection was granted by the Cheshire North and West Research Ethics committee on the 7th June 2010 (reference number 10/H1010/4). Ethical approval for phase 13 was granted by the Cheshire North and West Research Ethics committee on the 22nd December 2014 (reference number 14/NW/1484). The letters confirming ethical agreement for these phases of study are in Appendix 1. Participants gave written informed consent for data collection at multiple phases within the WCHADS. Information sheets that are relevant to the current thesis are given in Appendix 2.

## 2.2 WCHADS sampling strategy

The study used a two stage stratified design in which a consecutive general population sample (the 'extensive' sample) was used to generate a smaller 'intensive' sample stratified by psychosocial risk with more detailed measurement over time and both are followed in tandem. The aim of the extensive sample was to establish a consecutive general population sample for epidemiological study. Then the smaller intensive sample, over-representative of risk, was identified for more frequent and in-depth measurement. This approach allows general population estimates to be produced from data collected on intensive sample by using weighted analysis or maximum likelihood estimation with the stratification factors included in the modelling.

*2.2.1 WCHADS recruitment to the extensive sample*

The WCHADS sample was derived from a consecutive sample of 2158 first time pregnant mothers who enrolled at a NHS hospital antenatal clinic between February 2007 and October 2008. Women were approached at their 12-week appointment and asked if they would like to hear more about the study at their 20-week scan. Women were invited to participate in the WCHADS based on the following inclusion criteria: (i) primiparous, (ii) English speaking and (iii) 18 years of age or above at the time of recruitment. They were subsequently excluded if their baby had a gross congenital abnormality or did not survive. Multiple births were also excluded from further follow up. No exclusions were made on the basis of premature birth or low birth weight (<2500g), or late registration for antenatal care, as these events have been associated with prenatal stress in previous research. The figures for the recruitment to the extensive and intensive sample are presented in Figure 1, and described in more detail below.

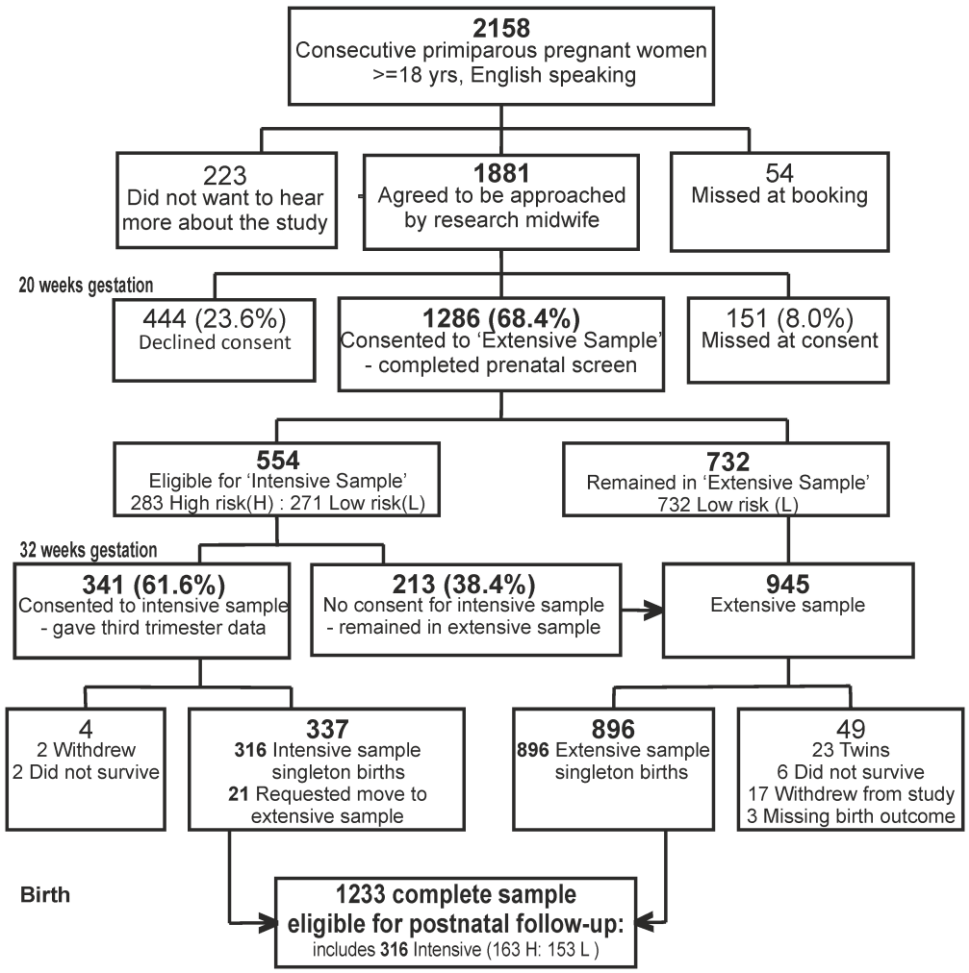


*Figure 2.1.* Recruitment to the extensive and intensive sample

*2.2.2 Extensive sample recruitment at phase 1*

In the first stage of recruitment, the consecutive sample of 1881 expectant mothers who had previously expressed interest in hearing more about the study at their 12 week scan (at their booking visit for antenatal care) were approached by research midwives at their 20 week scan and written informed consent to participate was requested. Consent was gained from 1286/1881 (68.4%) of those eligible. Expectant mothers who declined the invitation to participate at this phase were asked for their age and post code for demographic comparison purposes. Women who did not consent were significantly younger ($t(1927) = -5.3$, $p < .001$) and more deprived ($\chi^2(1) = 6.6$, $p < .01$) than those who consented. After written informed consent was gained, participants completed a short interview and questionnaire pack (phase 1).

*2.2.3 Intensive sample recruitment at phase 2*

During phase 1 all expectant mothers were informed that women reporting elevated levels of stress during pregnancy, and a subsample of those reporting lower levels of stress, would be contacted by researchers from the WCHADS team to be invited to take part in a more detailed part of the study. All researchers working for the WCHADS were, and remained, blind to the risk status of the participants in the sample. The intensive sample were stratified using a measure of psychological abuse in the partner relationship, the Dunedin Relationship scale (Moffitt, Caspi, Krueger, Magdol, Margolin, Silva, and Ros, 1997). The 20-item measure, completed at phase 1, assessed humiliating, demeaning or threatening utterances and behaviours in the partner relationship during pregnancy over the previous year. Both mother and partner perpetrated abuse was assessed by maternal report. A threshold of four or higher items endorsed for either mother or partner perpetrated abuse was set on the basis of data from the Dunedin Multidisciplinary study (Moffitt et al., 1997). Part way through a lower threshold was used of 3 or above to generate sufficient numbers for inclusion in the intensive sample. A total of 554 mothers were identified for invitation to the intensive sample, n = 283 who scored above threshold and a random sample of n = 271 who scored below threshold. The 554 women were contacted at 30 weeks gestation and given information about the intensive phase and were invited to arrange an appointment to consent to the intensive sample. 341 (61.6%) women consented to take part in the intensive study whilst 213 (38.4%) declined and either remained in the extensive sample or requested to withdraw. All those who consented

to the intensive sample were invited for interviews with trained research assistants between 32-36 weeks gestation.

### 2.3 Intensive sample assessment phases

The intensive sample completed antenatal interviews at 32 weeks (phase 2), a mother-infant lab assessment at 5 weeks (phase 4) and then mother-infant lab assessments and maternal interviews at the following ages: 7 months (phase 6), 14 months (phase 8), 2.5 years (phase 9), 5 years (phase 11) and 7 years (phase 13).

### 2.4 Extensive sample assessment phases

The extensive (including intensive) sample provided birth data (phase 3) and postal questionnaires at 9 weeks (phase 5), 14 months (phase 7) and 5 years (phase 12). They completed a home assessment at 3.5 years (phase 10) and then the extensive-only sample completed a home assessment at age 7 (phase 13).

### 2.5 Extensive sample additional reporter assessment phases

At phase 1, 7, 10, 12 and 13 fathers or father figures who were available and willing to take part completed postal questionnaires. At phase 13 class teachers completed postal questionnaires.

### 2.6 Sample attrition from birth to age 7

The extensive sample comprised 1,233 mothers with live singleton babies who were eligible for follow up. The intensive sample comprised 316 mothers. Retention in the intensive sample is high, with 272 (86.1%) of the original members of the intensive sample remaining intensive at age 7 years, and a further 9 moved to the extensive sample, creating a total of 88.9% overall retention in the study for the intensive sample. Attrition in the extensive sample has been greater. By age 7, the extensive sample comprised 908 consented participants (73.6% of the original 1,233) and data was collected from 778 participants (85.7% of those eligible).

## 2.7 Data collection phases used in this thesis

Chapter 3 uses mother questionnaire data from the phase 9, phase 11 and phase 12 assessment phases. Chapter 4 uses demographic data from phase 1, observed mother-infant data from phase 6, observed mother-infant data from phase 8 and mother questionnaire data from phase 9, 10 and 11. Chapter 5 uses demographic data from phase 1, observed child data from phase 11, mother questionnaire data from phase 11 and 13, and teacher questionnaire data from phase 13.

# Chapter 3: Measurement of callous-unemotional traits in very young children: a psychometric and validity study from 2.5 to 5.0 years[1]

[1] This paper has been submitted for publication as Wright, N., Sharp, H., Pickles, A., & Hill, J. (under review) Measurement of callous-unemotional traits in very young children: a psychometric and validity study from 2.5 to 5.0 years. *Assessment*

## 3.1 Abstract

Callous-unemotional (CU) traits are associated with severe and stable antisocial behaviour in childhood and adolescence. In order to understand the earliest origins of CU traits we need first to know whether the construct and measures are valid in young children. This study evaluated the psychometric properties and validity of a CU traits measure at age 2.5 years. The participants ($N$ = 775) were members of an epidemiological longitudinal study starting in pregnancy. Items from the Antisocial Process Screening Device and other problem behaviour scales were subjected to exploratory and confirmatory factor analysis. Structural equation modelling was used to test whether age 2.5 CU traits showed incremental validity in predicting aggression at age 5. The CU measure showed acceptable psychometric properties, factorial invariance by sex and good stability. Incremental prediction to later aggression was evident in girls, whereas boys showed strong continuity in aggression not found for girls.

*Keywords*: Callous-unemotional (CU) traits, physical aggression, preschool, incremental validity, sex differences

## 3.2 Introduction

Problems of oppositionality and aggression appearing in early childhood confer a substantially increased risk of later antisocial behaviour disorders and a wide range of psychiatric disorders including depression, anxiety and substance misuse (Odgers et al., 2008). While these early onset 'life course persistent' conduct problems share poor long term outcomes, it is likely that there is heterogeneity of risk factors and underlying processes (Hill, 2002). There is much current interest in a possible subgroup of conduct disordered children who show a lack of concern for the feelings of others and lack of guilt or remorse (Frick, 2009). In adults these traits are considered part of the affective dimension of psychopathy, and when applied to children they have been labelled as 'callous-unemotional traits' (CU traits). There is some evidence that there may be distinct developmental processes contributing to the development of conduct problems with and without CU traits. For example, conduct problems in children with CU traits have been found to be more highly heritable (Viding, Jones, Frick, Moffit & Plomin, 2008), less influenced by negative parenting practices (Pasalich, Dadds, Hawes & Brennan, 2012) and less responsive to typical conduct problem interventions (Hawes, Price & Dadds, 2014). Critically, CU traits in childhood and adolescence have been shown to be associated with more severe and enduring antisocial behaviour than conduct problems alone (Frick, Ray, Thornton & Kahn, 2014) supporting the utility of the application of the CU traits construct to childhood.

The majority of CU traits research has focused on samples aged 5-18 years, however, there is a small increasing literature examining whether CU traits can be reliably and validly measured in the pre-school period. Two domains of developmental research suggest that this may be so. First, observational studies have identified that empathy-related behaviours and guilt emerge during the first and second years of life (Kochanska, Gross, Lin & Nicholas, 2002; Vaish, Carpenter & Tomasello, 2009) which suggests that meaningful variations in CU traits may be measureable as early as age 2 years. Second, trajectories of elevated aggressive behaviour have also been demonstrated to start in the second year of life (Tremblay et al., 2004; Campbell et al., 2010) and if CU traits play a causal role in the

development of persistent aggressive behaviour, then CU traits or their precursors may be measurable and operating at this early age too. Identifying the earliest age at which CU traits can be reliably measured has important implications for research examining the developmental pathways to and from CU traits and for the development of potential preventative intervention before severe antisocial behaviour develops.

Two different approaches to measurement of CU traits in young children have been adopted in the field. In the first, standard measures of CU traits developed for older children and adolescents have been modified for preschool use. The most commonly used are the Antisocial Process Screening Device (APSD; Frick & Hare, 2001) which contains a 6 item CU subscale, and the Inventory of Callous-Unemotional traits (ICU; Frick, 2004), a 24 item measure developed by creating multiple items from four of the six APSD items considered to be the most key to the CU construct. Both measures have been modified for preschool use by replacing reference to 'school-work' with 'structured activities'. The second approach involves using a collection of items drawn from existing measures of early child behaviour (hybrid measures). This method has the advantage that items were developed specifically for younger children and so possess more face validity for this age group than items from measures developed for older children. However, they lack the background of validation and replication which characterises the existing CU traits measures.

### *3.2.1 Factor structure of CU measures in early childhood*

An important initial question when considering CU traits measurement in very young children is whether raters can reliably distinguish CU traits behaviours from other problem behaviours (Willoughby, Mills-Koonce, Gottfredson & Wagner, 2014). This has been examined using exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) on CU traits items and items from other child problem behaviour dimensions. In the first of these studies, Dadds, Hawes, Frost and Fraser (2005) demonstrated that the APSD CU items were separable from the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) conduct problems, hyperactivity, anxiety and peer problems in a community sample of 1,359 4-9 year

olds using EFA. Three studies of three year olds have subsequently used CFA on items from the Child Behaviour Checklist (CBCL; Achenbach & Rescola, 2001) and demonstrated that a 5 item CU traits subscale was distinct from ODD and ADHD (Waller, Hyde, Grabell, Alves & Olson, 2015; Willoughby, Waschbusch, Moore & Propper, 2011; Willoughby et al., 2014). This question has yet to be examined in children under the age of 3. In this study we test whether mothers can reliably distinguish CU traits from other childhood problem behaviours at age 2 by employing CFA to test whether two separable factors reflecting CU traits and aggression are clearly identifiable.

### *3.2.2 Reliability of CU traits measures in early childhood*

A key issue in CU traits measurement in both younger and older samples (e.g. Essua, Sasawaga & Frick, 2006) has been that measures tend to show poor internal consistency reliability. The majority of studies of early childhood have reported unsatisfactory Cronbach's Alpha for their measures. For example, α = .54 reported for the APSD from a sample of 2-5 year olds (Kimonis et al., 2006) and α = .55 to .66 reported for CBCL-based CU traits measure in four samples of 3-4 year olds (Kimonis, Bagner, Linares, Blake & Rodriguez, 2014; Waller et al., 2015; Willoughby et al., 2011; Willoughbly et al., 2014). In the only investigation to assess the psychometric properties of a CU traits measure in 2 year olds, Hyde et al. (2013) reported an unsatisfactory Cronbach's Alpha at age 2 years (α = .57 for primary caregiver and α = .47 for alternative caregiver report), which was slightly improved by age 3 years (α = .64 and α = .66) and approaching commonly accepted values for both reporters at age 4 (α = .72 and α = .66) for their 5 item hybrid measure. This led Hyde et al. to conclude that CU traits may be sufficiently developed to assess at age 2 years. However, this conclusion may be premature given this is the only study to date to examine CU traits in 2 year olds, and other studies of 3 and 4 year olds using short measures of CU traits have reported similarly low Cronbach's Alpha levels. Further, in this study the measure comprised items assessing deceitful or manipulative behaviours which are not typically included in measures of CU traits in childhood, such as the APSD or the ICU, which focus instead on lack of guilt and empathy and poverty of affect. Of course, lying and manipulativeness are relevant behaviours seen

in adolescence and adulthood but they are likely to require more advanced cognitive abilities than those normally developed at age 2. This developmental and conceptual issue likely contributed to the poorer performance of their measure at age 2 specifically.

One investigation has employed the 24 item CU traits measure, the ICU, with a sample of 3 year olds with repeated measurement at age 4 ($n$ = 622; Ezpeleta, Osa, Granero, Penelo & Domenech, 2013) and reported satisfactory Cronbach's Alpha for the subscales and total score at both ages ($\alpha$ = .79 to $\alpha$ = .93 for the subscales and total scores). With a measure designed to assess psychopathic traits in children, Colins et al. (2014) reported a Cronbach's Alpha of .95 for a 10 item CU traits subscale in a subsample of 687 3 year olds. Hawes and Dadds (2007) reported improved internal consistency (Cronbach's Alpha = .79) in a mixed age sample of 4-8 year olds after supplementing the APSD with the SDQ prosocial items (reverse coded). It is well known that the Alpha coefficient is affected by the number of items in a scale, with fewer items often yielding lower values (Cortina, 1993). In light of this, in this study we use the APSD as a recognised foundational CU traits measure but we also follow the approach of Dadds and colleagues and supplement it with items from other problem behaviour scales designed for young children in order to establish a measure that adequately assesses the construct of CU traits at age 2 and age 5.0, includes a broader range of items and shows acceptable psychometric properties, particularly satisfactory internal reliability. We also report an alternative and more appropriate method of assessing internal consistency, Ordinal Alpha. Cronbach's Alpha is based on the Pearsons correlation matrix and so is best suited to items rated on a continuous scale. Ordinal Alpha, which is based on the polychoric correlation matrix, is more appropriate for use with items rated on an ordinal scale (Zumbo, Gaderman & Ziesser, 2007) which most child problem behaviour measures are.

### *3.2.3 Stability of CU measures across early childhood*

CU trait scores have been shown to be moderately stable across childhood and from childhood to adolescence (Frick et al., 2014). To date the findings from studies of early childhood have also supported moderate to high stability in CU traits.

Hyde et al. (2013) reported a correlation of .47 between their age 2 and 3 deceitful-callous measures. Ezpeleta et al. (2013) found moderate stability in ICU scores from age 3 to 4 years (ICC = .53 for total and ICC = .51-.53 for subscales). Over a longer period from 3 to 5 years, Willoughby et al. (2011) reported a latent factor correlation of .84. In this study we examine stability from age 2.5 to 5.0.

### *3.2.4 Validity of CU traits measures in early childhood*

The key hypotheses regarding the clinical significance of CU traits focus on their role in disinhibiting violence and physically aggressive behaviour (e.g. the Violence Inhibition Mechanism; Blair, 1995). In particular CU traits are postulated to underpin proactive aggression (Frick, Cornell, Barry, Bodin & Dane, 2003). Whilst studies of the validity of psychopathy and CU traits in adults and adolescents examine criminal outcomes, such as violent versus non-violent crimes, these are not yet relevant in young children and so it is necessary to focus on the prediction of developmentally relevant behaviours, such as physically aggressive behaviour. The key test of the validity of CU traits in predicting antisocial outcomes is whether they show incremental prediction over and above other known predictors (Frick et al., 2014) such as initial problem behaviour. We examine the incremental prediction of physical aggression at age 5 years accounting for age 2.5 physical aggression.

Associations between CU traits and physical aggression have been reported in at least three early childhood studies, but none have examined the incremental prediction of aggression. Kimonis et al. (2006) found prospective prediction from mother-report on the APSD to teacher-reported aggression 6 months later with a sample of 2-5 year olds. Ezpeleta et al. (2013) demonstrated both cross-sectional and prospective associations from age 3 to 4 years between teacher-reported CU traits and aggression. Willoughby et al. (2014) found age 3 CU traits measured using the CBCL to predict persistent teacher-reported aggression from age 6-12 years, but only in interaction with ODD and disorganised attachment status. Two studies have examined the incremental prediction of CU traits but to broad behaviour problems outcomes only. Hyde et al. (2013) found their age 3 deceitful-callous measure to predict increased behaviour problems from age 2 to 4 years after accounting for initial problem behaviour. Further, Waller et al. (2015) found age 3 mother-reported CU traits predicted teacher-reported externalizing problems at age 6, after accounting

for age 3 externalizing problems. No study has yet shown incremental validity for a CU trait measure in 2 year olds in this way.

### *3.2.5 CU traits measurement and the possible role of sex differences*

Whether CU traits show sex differences in associations with outcomes has been given relatively little consideration in the literature, and none of the studies of early childhood have examined for sex differences. It is well-established that boys show higher mean levels of CU traits than girls (Ezpeleta et al., 2013; Fanti & Kimonis, 2013; Marsee, Silverthorne & Frick, 2005). Levels of physical aggression are also lower in girls (Card, Stucky, Sawalani & Little, 2008) even at age 2-3 years (Baillargeon et al., 2007). Some studies have examined associations between CU traits and aggression separately for boys and girls and found them to be similar (Essau et al., 2006; Kimonis et al., 2006; Silverthorne, Frick & Reynolds, 2001) although significant sex by CU interactions have been reported by others (Fanti & Kimonis, 2013; Thornton, Frick, Crapanzano & Terranova, 2012) Very few studies have sought to establish that CU measures are invariant across sex before examining associations with outcomes, and therefore any sex difference findings reported may be due to measures operating differently in boys and girls. In this study we test whether the CU traits measure that we generate is invariant across sex, and then examine whether there are sex differences in associations between CU traits and aggression. We make no specific hypotheses regarding sex differences.

### *3.2.6 The present study*

In summary, in the current prospective longitudinal study, CU traits and physical aggression were assessed at age 2.5 and again at 5.0 years. The first step was to establish CU traits scales at each age point with satisfactory psychometric properties, including internal reliability and measurement invariance by sex. We examined whether parents could reliably distinguish CU traits and aggression by testing two-factor CU traits and aggression models against one-factor models. CFA was also used to examine whether there were continuities in CU traits from age 2.5 years to

5.0 years. The main analysis used structural equation modelling to examine concurrent and prospective associations between CU traits and physical aggression at 2.5 years and 5.0 years. Our key hypothesis was that age 2.5 CU traits would show incremental validity in predicting physical aggression at age 5.0 years after accounting for age 2.5 physical aggression and all other possible prospective and cross-sectional associations, and that this did not differ by sex of child.

## 3.3 Method

### *3.3.1 Sample*

Participants were mothers and children taking part in the Wirral Child Health and Development Study, a prospective epidemiological cohort study starting in pregnancy designed to investigate the earliest origins of childhood conduct problems. All women gave written informed consent at the point of recruitment in the antenatal clinic. The study used a two stage stratified design in which a consecutive general population sample (the 'extensive' sample) is used to generate a smaller 'intensive' sample stratified by psychosocial risk with more detailed measurement over time and both are followed in tandem (Sharp et al., 2012). Mother's responses to a questionnaire at 20 weeks of pregnancy (recruitment) assessing psychological abuse in their current or recent partner relationship (Moffitt et al., 1997) were used to generate the stratified intensive sample of mothers for more detailed study. The stratification variable was chosen for its known association with a variety of risk factors for early child development. The whole cohort comprised 1233 women of mean age at recruitment of 26.8 years (*SD* = 5.8, range 18-51) and 41.8% of the sample were in the most deprived quintile of UK neighbourhoods (Noble et al., 2004). There were 316 mothers recruited to the intensive sample at 32 weeks pregnancy. This report uses questionnaire data collected from the whole cohort who gave data at 20 weeks pregnancy and again at age 5.0 years (*n* = 775), and from the stratified intensive sub-sample at 2.5 years (*n* = 241). Nonresponse at age 5 was associated with younger maternal age ($U(N = 1233) = 230{,}692$, $Z = 8.67$, $p < .001$) and living in the most deprived quintile of UK neighbourhoods ($\chi^2(1, N = 1233) =$

19.62, $p < .001$). The mean age of the children at the 2.5 year assessment was 30.86 months (*SD* = 2.31, range = 27 - 42 months) with slightly more girls (*n* = 123) than boys ( = 118), and the mean age of all 775 children whose mothers completed questionnaires at 5.0 years was 58.64 (*SD* = 3.74, range = 49 - 73 months) with 402 girls and 373 boys. At age 5.0, 80% of mothers were either married or cohabiting, 4.8% had a partner living elsewhere and 15% were single.

### *3.3.2 Measures*

*CU traits.* Items were drawn from four different child problem behaviour scales, shown in Table 3.4.1.1. Items were selected based on inclusion in CU traits measures in other studies (Dadds et al., 2005; Hyde et al., 2013; Kimonis et al., 2014; Willoughby et al., 2011) and relevance to the CU traits construct, with a focus on items assessing lack of concern for others, lack of guilt and poverty of affect. All six items from the CU subscale of the APSD were selected for use at both time points (2.5 years and 5.0 years). APSD items are rated on a 3 point scale: 0 = *not true,* 1 = *sometimes true*, 2 = *very true.* Consistent with previous use of the measure with younger samples, the subscale showed somewhat low Cronbach's Alpha ($\alpha = .56$ at age 2.5 years and $\alpha = .60$ at age 5.0 years). Six items were selected from the CBCL at both time points. The item 'doesn't seem to feel guilty after misbehaving' was not included due to similarity to the APSD item 'feels bad or guilty when he/she does something wrong'. CBCL items are rated on a 3-point scale: 0 = *not true/never*, 1 = *somewhat true/sometimes*, 2 = *very true/very often.* At age 5.0, all 5 items from the prosocial subscale of the SDQ were selected, based on the University of New South Wales system of combining items from the APSD with the SDQ prosocial items (Dadds et al., 2005). One item from the Brief Infant Toddler Socio-emotional Assessment (BITSEA; Briggs-Gowan, Carter, Irwin, Wachtel & Cicchetti, 2004) "tries to help when someone is hurt (for example, gives a toy)" was included at age 2.5 based on its similarity to the SDQ prosocial items. A total of 13 items were selected for age 2.5 years and 17 items for age 5.0 years. EFA and CFA were run separately for age 2.5 and 5.0 years and the CU factor composition was allowed to differ at each age to allow for developmental differences in the manifestation of CU traits.

*Physical aggression.* Mothers completed a physical aggression questionnaire (Baillargeon et al., 2007) at age 2.5 years and 5.0 years. The questionnaire consists of five items previously shown to yield aggression scores with stability from ages 17 to 29 months (Baillargeon et al., 2007). Each item is rated on a three-point scale: 0 = *not true*, 1 = *somewhat or sometimes true*, 2 = *very true or often true*. The Cronbach's Alpha in the present sample was adequate for age 2.5 years ($\alpha = .67$) and 5.0 years ($\alpha = .82$).

### *3.3.3 Analysis plan*

First, the CU items were entered into an exploratory factor analysis for ordinal data (using the weighted least squares mean adjusted estimator [WLSM] and promax rotation) in Mplus version 7 (Muthen & Muthen, 2012) separately for age 2.5 and age 5.0 years. Items with a factor loading >.35 were retained. Second, a series of multi-group two-factor CFA, estimated using the WLSMV estimator and Theta parameterization, examined measurement invariance across sex in CU traits and aggression. In model 1 (configural model) the pattern of factor loadings were constrained to be the same for boys and girls, testing that the same items formed the CU and aggression factors across sex. In model 2 (metric model) the individual factor loadings were constrained to be the same, testing whether the contribution of individual items varies by sex (weak factorial invariance). In model 3 (scaler model) the thresholds were also constrained to be the same, to examine whether the items performed the same across sex (strong factorial invariance). Full invariance is demonstrated when the placing of additional constraints on the model does not produce a significant worsening in model fit. The *DIFFTEST* command was used to evaluate whether a substantial change in model fit occurred as a result of imposing additional constraints, as well as the CFI change ($\Delta$CFI). A non-significant chi-square difference test and a small CFI change (in which a decrease is no greater than .01) are considered indicative of invariance (Cheung & Rensvold, 2002). If a significant chi-square difference test is found, the modification indices are examined to determine which items failed the strong factorial variance assumption. In the absence of modification indices the individual items are checked for those showing the largest difference between boys and girls. The thresholds of these items are then

allowed to vary freely and model fit is re-examined as a test of partial strong factorial invariance.

Third, two CFA models were estimated and compared using the DIFFTEST command, to test whether a one-factor or two-factor CU and aggression model best fit the data. Finally, two multi-group (by child sex) structural equation models (SEM) for ordinal data were fitted to examine cross-lagged continuity in CU traits and aggression from age 2.5 to 5.0 years, concurrent associations with aggression at each age, and the prospective association between CU traits at age 2.5 and aggression at age 5.0 years, and vice versa. We used the WLMSV estimator in order to include whole cohort at age 5.0 and the intensive sub-sample at age 2.5 years within a single model. To account for sample stratification of the intensive sub-sample we included the measure on which the stratification was based as an auxiliary variable (Graham, 2003). We fitted the model of Figure 1 in which we imposed a common measurement model constraining the factor loadings, measurement errors, and thresholds to be the same across boys and girls and with the factor loading for the first factor fixed at 1 for identification. However, in order to check for sex differences we allowed the means, variances and covariances among the factors to differ by sex of child. The model provided estimates of the effects of time 1 (age 2.5) scores on time 2 (age 5.0) scores, both the simple lagged effects of early CU on later CU traits and aggression on later aggression, and, in order to test the main hypothesis, the cross lagged effects of early CU traits on later aggression, and early aggression on later CU traits. This constrained model gave common estimates of these effects, assuming that a unit change in age 2.5 CU traits or aggression had the same effects on age 5.0 CU traits and aggression in both boys and girls. A second unconstrained model was run allowing the coefficients for girls to be different from those for boys, and the constrained and unconstrained models were then compared using the DIFFTEST.

The adequacy of all CFA and SEM models was assessed using the Root Mean Square Error (RMSEA) criterion where less than 0.05 is considered a good fit and less than .08 considered reasonable fit, and the Comparative Fit Index (CFI) where values above .95 indicate good fit and .90 reasonable fit (Marsh, Hau, & Wen, 2004).

To avoid numerical problems associated with sparse data in the multivariate model, where endorsement rates were < 1.5%, scores of 1 and 2 were collapsed to create binary variables. This was applied to the CU traits items 'cruel to animals' 'selfish, and 'shows little affection' at 2.5 years and 5 years, and to 'unresponsive to affection', 'volunteers to helps others' (reverse coded), 'kind to others' (reverse coded) and 'considerate to others' (reverse coded) at 5 years only. Similarly all of the physical aggression items at both ages, except 'gets in many fights' at 2.5 years months which had not received a '2' response, were collapsed to create binary variables. Although this generated adequate cell sizes in the sample as a whole, the analytic approach required adequate numbers in both males and females. In females cell sizes were small for 'gets in many fights' at age 2.5 years and 'bites other children' at age 5 years. "Gets in many fights" was combined with the similar item "physically attacks others", and "bites other children" was combined with the next rarest item "kicks other children". The items were combined at both ages to ensure consistency in the physical aggression latent variable across the two ages. Inter-item correlations were added to the CFA and SEM models for items from the same measure to attempt to account for method effects. The item 'cruel to animals' showed a negative residual variance at age 2.5 in the multivariate model and so the variance was fixed to .01.

## 3.4 Results

### *3.4.1 Exploratory factor analysis on the CU items*

*Age 2.5 years***.** The 13 CU items were entered into an EFA. The APSD item "Does not show feelings or emotions" showed problems with empty cells in the cross-tabulation with two CBCL items ("Shows little affection toward people" and

"Seems unresponsive to affection") and thus was removed from the EFA. This item has shown poor item-total correlations with the other APSD items (Poythress et al., 2006) and failed to load in factor analysis (Dadds et al., 2005). Eigenvalues for the first three factors were 4.6, 1.6, and 1.1, and the scree plot supported a one factor solution. The CBCL item "Shows too little fear of getting hurt" gave a factor loading <0.35 and was dropped, resulting in 11 items at age 2.5 years.

*Age 5 years.* The EFA for the 17 CU items gave eigenvalues of 7.1, 1.6 and 1.2, and the scree plot supported a one-factor solution. The item APSD "Does not show feelings or emotions", gave a factor loading <0.35 and so was omitted, resulting in 16 items at age 5.

### *3.4.2 Confirmatory factor analyses*

*Age 2.5 years measurement invariance.* The 11 items retained at age 2.5 were then tested for measurement invariance across boys and girls using multi-group CFA. Model 1, the configural model, showed good fit (RMSEA = .05, CFI = .95). The fit improved in model 2 where factor loading invariance was introduced (RMSEA = .04 CFI = .96) with a non-significant chi-square difference test. Threshold invariance was introduced with model 3 and the fit was largely unchanged (RMSEA = .04, CFI = .95) the chi-square tests comparing model 3 to model 1 and 2 were both non-significant, demonstrating strong scalar or strong factorial invariance. The full model fit and comparison results are presented in Table 3.6.1.1 (supplementary material).

*Age 5 years measurement invariance.* The 16 items retained at age 5 were then tested for measurement invariance across sex. Model 1, the configural model, showed good fit (RMSEA = .05, CFI = .95). However, the modification indices indicated that items 'APSD: does his/her best in structured activities' and 'CBCL: selfish' should cross-load on the aggression factor for boys and girls, and 'CBCL: shows too little fear' should cross-load for boys. These three items were not considered central to the CU traits construct, and cross-loading with aggression was undesirable given the aim of examining a purely physical aggression outcome, therefore, the items were removed. A further configural model (Model 1b) was tested

on the remaining 13 items and showed improved fit (RMSEA = .03, CFI = .99) with no further modification indices, and so this model was used in further analysis. The introduction of factor loading invariance with model 2 resulted in a further improvement in fit (RMSEA = .02, CFI = .99) with a non-significant chi-square difference test. However, the introduction of threshold invariance in model 3 resulted in a significant chi-square difference test ($p$ = .003) and therefore strong factorial invariance was not achieved. There were no modification indices above the minimum value so individual item thresholds were inspected for differences between boys and girls. Items 'CBCL: hits other children', 'CBCL: seems unresponsive to punishment', 'APSD: keeps the same friends' and 'SDQ: volunteers to help' all showed a difference of > 0.4, with boys showing a lower threshold than girls on all items apart from 'volunteers to help', and so the thresholds for those items were freed. The chi-square test for difference testing between the metric and partial scaler models was now non-significant ($p$ = 0.08) therefore we found evidence for partial strong or partial scalar invariance at age 5 years. The full model fit and comparison results are presented in Table 3.6.1.2 (supplementary material).

*One- versus two-factor CU traits and aggression CFA models.* We next examined whether mothers could differentiate CU traits and aggression by comparing a one-factor CFA model where all the CU and aggression items loaded on one factor, to the two factor model, using the chi-square DIFFTEST. The model fit statistics and model comparison results are displayed in Table 3.4.2.1. The two-factor model showed the best fit at age 2.5 years (RMSEA = .05, CFI = .95) and 5.0 years (RMSEA = .05, CFI = .94) and the chi-square difference tests indicated that the two-factor models showed significantly better fit ($p$ < .001 for both ages). The standardised factor loadings are displayed in Table 3.4.1.1.

### *3.4.3 Internal consistency*

Cronbach's Alpha for the CU traits measure at age 2.5 years was α = .72 and age 5.0 years α = .83. Ordinal Alpha, a more appropriate index of internal consistency for items rated on an ordinal scale, was α = .87 for age 2.5 years and α = .89 for 5.0 years.

### *3.4.4 Sex differences in mean levels*

Having established measurement invariance we then used multi-group CFA to test for sex differences in the means on the latent variables. At age 2.5, boys scored significantly higher on CU traits (-.34, $p$ = .041) but not aggression (-.32. $p$ = .198), whereas at age 5 boys scored significantly higher on both CU traits (-.32, $p$ = .002) and aggression (-.35, $p$ = .006).

### *3.4.5 Stability for boys and girls*

Factor correlations between age 2.5 and 5.0 year CU traits were similar and substantial for boys and girls (.75, $p$ < .001 and .71 $p$ < .001) with a somewhat larger association over time for aggression in boys (.59, $p$ <.001) than for girls (.35, $p$ < .001).

Table 3.4.1.1 *Standardised Factor Loadings from the Two-Factor CU traits and Aggression Models at Age 2.5 and 5.0 years*

| Items | Age 2.5 | Age 5 |
|---|---|---|
| CU traits items | | |
| APSD 1: Concerned about the feelings of others (R) | .48 | .47 |
| APSD 2: Seems motivated to do his/her best in structured activities (R) | .61 | |
| APSD 3: Is good at keeping promises (R) | .54 | .47 |
| APSD 4: Feels bad or guilty when he/she does something wrong (R) | .43 | .62 |
| APSD 5: Keeps the same friends (R) | .36 | .61 |
| APSD 6: Does not show emotions | | |
| CBCL 14. Cruel to animals | .99 | .60 |
| CBCL 58: Punishment doesn't change his/her behavior | .62 | .72 |
| CBCL 67: Seems unresponsive to affection | .77 | .77 |
| CBCL 69: Selfish or won't share | .42 | |
| CBCL 70: Shows little affection toward people | .48 | .84 |
| CBCL 72: Shows too little fear of getting hurt | | |
| BITSEA 22. Tries to help if someone is hurt (R) | .69 | |
| SDQ 1: Considerate of other people's feelings (R) | | .75 |
| SDQ 4: Shares readily with other children (R) | | .53 |
| SDQ 9: Helpful if someone is hurt, upset or feelings ill (R) | | .57 |
| SDQ 17: Kind to younger children (R) | | .60 |
| SDQ 20: Often volunteers to help others (R) | | .46 |
| Aggression items | | |
| Hits other children | .76 | .87 |
| Bites other children/Kicks other children | .75 | .87 |
| Gets in many fights/Physically attacks others | .87 | .90 |

*Note.* CBCL = Child Behavior Checklist (CBCL), APSD = Anti-Social Processes Screening Device, BITSEA = Brief Infant Toddler Social and Emotional Assessment (BITSEA), SDQ = Strengths and Difficulties Questionnaire (SDQ) .

Table 3.4.2.1 *Fit statistics and results of DIFFTEST for one versus two factor CU and aggression models*

| | χ2 (df) | CFI | RMSEA | χ2 DIFFTEST |
|---|---|---|---|---|
| Age 2.5 years | | | | |
| 1 factor | 104.91(57)*** | .92 | .06 | |
| 2 factor CU and aggression | 83.25(56)* | .95 | .05 | 16.01(1)*** |
| Age 5 years | | | | |
| 1 factor | 677.29(152)*** | .91 | .07 | |
| 2 factor CU and aggression | 275.08(151)*** | .95 | .05 | 54.94(1)*** |

***p<.001, *p<.05.

*3.4.6 Multivariate model to examine incremental validity*

We fitted the model shown in Figure 1, and more fully described in the Methods section, to data from both boys and girls, constraining the four path coefficients between the factors to be the same for boys and girls. The model fitted well (RMSEA = .03 (CI .02 – .03) CFI = .93). We next fitted a model in which the path coefficients were allowed to be different, assessing any improvement in fit using the DIFFTEST. While overall fit statistics remained unchanged the DIFFTEST was highly significant, indicating a clear sex difference ($X^2$ (4) = 10.95, $p$ = .028) when all the paths were considered. Figure 1 shows the magnitudes of the standardized coefficients where it is evident that the sex differences were of two kinds. There was continuity of aggression from 2.5 to 5.0 years in boys (.84, $p$ = .006) but not girls (.02, $p$ = .923). By contrast the cross-lagged path from CU traits at 2.5 years to physical aggression at 5.0 years was substantial in girls (.62, $p$ < .001) but entirely non-significant for boys (-.06, $p$ = .933). There was no sex difference in continuities from CU traits at 2.5 years to CU traits at 5 years, which was significant for both boys (.74, $p$ < .001) and girls (.81, $p$ < .001). Cross-sectional correlations between the

CU traits and aggression factors at age 2.5 were similar for boys (.71) and girls (.58) and this was the case also at age 5 years (.75 and .76 respectively). Combining the various effects together the model estimated that at age 5 years for boys 43% of the variation in the CU factor and 36% of variation in the aggression factor was explained by the measures at age 2.5. The corresponding values for girls were 50% for CU traits and 60% for aggression.

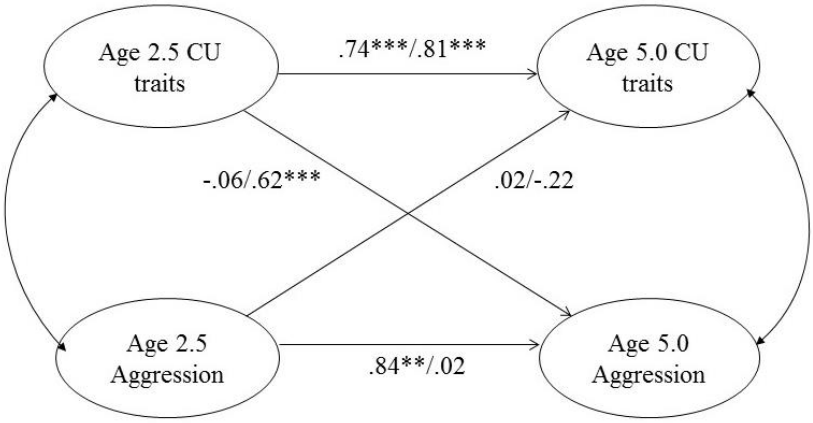


*Figure 3.4.6.1.* Standardised path estimates and covariances for CU traits and aggression at age 2.5 and 5.0 years; ** = p < .01, ***=p<.001; paths are shown for boys/girls; the observed indicators for the latent variables (circles) are not shown

## 3.5 Discussion

In this study we sought to establish whether CU traits can be measured reliably at 2.5 years, and to assess their validity at this age as evidenced in an incremental prediction of physical aggression from 2.5 to 5.0 years. We measured CU traits in children aged 2.5 years by supplementing a widely used measure of CU traits, the APSD, with items from other problem behaviour scales for young children. This yielded a CU traits scale invariant across sex with satisfactory psychometric properties that showed strong stability from age 2.5 to 5.0 years for both boys and girls. CU traits and aggression showed significant and substantial associations at age

2.5 and 5.0 years for both boys and girls in line with theory. We found that for girls only, CU traits at 2.5 years predicted physical aggression at 5.0 years after accounting for age 2.5 aggression and all other possible cross-sectional and prospective associations.

As outlined earlier, establishing whether CU traits can be identified in young children is a priority if their role in early onset of aggression is to be studied. There are however substantial issues regarding their measurement that were examined in this study. First, in response to the concern that CU traits may not be identifiable as separable from conduct problems, we showed using CFA that mothers' ratings of CU traits were separable from ratings of physical aggression at age 2.5 years. This builds on previous findings which have demonstrated that CU traits are distinct from other problem behaviour dimensions at age 3 years and above (Willoughby et al., 2011; Willoughby et al., 2013; Waller et al., 2015). Second in order to deal with problems of low internal consistency, we supplemented an established measure of CU traits with items from other child problem behaviour scales and this yielded a measure with satisfactory internal consistency. Third given increasing interest in the possibility that there are sex differences both in the origins and consequences of the CU traits, we examined measurement invariance across boys and girls and found strong invariance for the age 2.5 measure and partial strong invariance for the age 5.0 measure. Very few studies have examined measurement invariance by sex for CU traits measures; our findings are consistent with the only previous study to examine measurement invariance in an early childhood sample, which demonstrated invariance by sex for the ICU at ages 3 and 4 years (Ezpeleta et al., 2013). Finally we examined incremental validity in the prediction of aggression at 5.0 years from CU traits at 2.5 years, making use of the measurement invariance that we had established to test for sex differences. We found age 2.5 CU traits to predict age 5.0 aggression over and above age 2.5 aggression and all other possible cross-sectional and prospective associations, but in girls only.

Strengths of the study included consecutive recruitment from an antenatal clinic serving a defined geographical area, enabling effect estimates applicable to the general population to be generated. In contrast to many studies of CU traits the behavioural outcome was child aggression which is most relevant to key hypotheses

regarding the effects of CU traits on behaviour (Blair, 1995). Structural equation modelling (SEM) which has rarely been used in studies of links between CU traits and aggression conferred four main advantages including, first it utilized an item level analysis which takes account of differing contributions of items, second it enabled all possible prospective pathways to be examined simultaneously, third it allowed measures to operate differently over time or by sex, and fourth it provided tests of sex differences. A limitation of SEM with this sample was that, as a result of some sparse cells, it was necessary to collapse some items to binary variables, and for the aggression latent variable, to combine items. A further limitation of the study was that all of the measures were mother-report questionnaires and so the findings may be influenced by common method variance. Finally, we conducted both EFA and then CFA on the same sample which is problematic as a factor structure derived from an EFA will almost always fit well in a CFA using the same data. We chose to start with EFA as we thought it important to be confident that a more exploratory unstructured analysis did not suggest something very different from expectation. Unfortunately the sample size at age 2.5 years was not large enough to split in two to perform EFA on one half and then CFA on the second half of the sample.

The prediction from CU traits at 2.5 years to peer aggression at 5.0 years additional to the prediction from 2.5 years aggression in girls, but not in boys, needs to be considered in relation to the finding from the same analyses, that the continuity in aggression from 2.5 years to 5.0 years was much stronger in boys than in girls. This is consistent with findings from large scale studies of older children that boys are more likely than girls to show stable aggression (Campbell et al., 2010; Lee et al., 2007), and with similar evidence from smaller scale studies of preschool children (Alink et al., 2006, Cummings, Iannotti & Zahn-Waxler, 1989). Here we report the same phenomenon in a large preschool sample, and specifically in relation to peer aggression, further supporting the possibility that the emergence and maintenance of early childhood aggression may be underpinned by different processes in boys and girls (Crick & Zahn-Waxler, 2003). Thus one possible interpretation of the failure to show an incremental effect of CU traits in boys is that the extent of change in aggression over the period 2.5 years to 5.0 years, either increasing or decreasing, was so limited that there was little for CU traits to explain. The question is then posed as to whether the key risk processes for aggressive behaviours in boys are to be found before age 2.5 years, with a challenge to identify CU traits or their precursors during

infancy or the toddler period. There may also be other explanations for the sex difference such as that the translation of CU traits into aggression is dependent on other influences, for example, deficits in behavioural inhibitory processes, so that even in the absence of main effect, effects may be found in interaction with other variables. Equally the CU traits construct may not be valid in young boys because the relevant empathic processes develop later in boys than girls (Rhee et al., 2013), or the measure may not be valid because the behaviours that reflect CU traits are not identified in the items of our existing measures.

In conclusion, this study showed that a measure of CU traits can be constructed that meets current concerns about poor psychometric properties of measures of CU traits in very young children, and that measures a construct that is distinct from aggression. Studies of sex differences at this age can be conducted with confidence that items have the same relationship to the latent variable in boys and girls. The marked sex difference, both in stability of aggression and prediction from CU traits, may reflect different pathways to aggression in boys and girls, or differences in validity of the CU traits construct or measure in boys at 2.5 years. Designs of early intervention studies to prevent CU traits will need to account for the possibility that therapeutic approaches may need to vary by sex of the child, and that measurement of early CU traits outcomes may not mean the same in boys and girls.

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3.6 Supplementary material

Table 3.6.1.1: *Age 2.5 years CFA models testing measurement invariance across sex*

| | **Parameters** | **Chi2(df)** | **p** | **RMSEA** | **RMSEA 90% C. I** | **CFI** |
|---|---|---|---|---|---|---|
| Model 1: configural | 114 | 141.704(110) | .023 | .049 | .020 - .071 | .945 |
| Model 2: metric | 100 | 148.170(124) | .069 | .040 | .000 - .063 | .958 |
| Model 3: scalar | 83 | 167.275(141) | .065 | .039 | .000 - .061 | .954 |
| **Model 1 vs Model 2** | | 14.886(14) | .444 | | | |
| **Model 1 vs Model 3** | | 31.886(31) | .422 | | | |
| **Model 2 vs Model 3** | | 14.763(17) | .612 | | | |

Table 3.6.1.2: *Age 5 years CFA models testing measurement invariance across sex*

| | **Parameters** | **Chi2(df)** | **p** | **RMSEA** | **RMSEA 90% C. I** | **CFI** |
|---|---|---|---|---|---|---|
| Model 1a: configural | 166 | 471.884(232) | .001 | .052 | .045 - .058 | .947 |
| Model 1b: configural **(modified)** | 126 | 199.678(160) | .018 | .025 | .011 - .036 | .989 |
| Model 2: metric | 113 | 195.972(113) | .111 | .019 | .000 - .030 | .994 |
| Model 3a: scalar | 92 | 237.694(194) | .018 | .024 | .011 - .034 | .988 |
| Model 3b: Scalar **(modified)** | 190 | 218.987 | .073 | .020 | .000 - 031 | .992 |
| **Model 1b vs Model 2** | | 9.379(13) | .744 | | | |
| **Model 1b vs Model 3a** | | 50.215(21) | .003 | | | |
| **Model 1b vs Model 3b** | | 28.890(3) | .523 | | | |
| **Model 2 vs Model 3b** | | 25.764(17) | .079 | | | |

# Chapter 4: Maternal sensitivity to distress, attachment and the development of callous-unemotional traits in young children[2]

[2] This paper has been submitted as Wright, N., Hill, J., Sharp, H., & Pickles, A. (under review). Maternal sensitivity to distress, attachment and the development of callous-unemotional traits in young children. *Journal of Child Psychology and Psychiatry.*

## 4. 1 Abstract

Background: Callous-unemotional (CU) traits are characterized by a lack of responsiveness to the emotions of others, particularly negative emotions. A parenting environment where the child's own distress emotions are sensitively responded to may help foster the child's ability to respond to the emotions of others. We tested whether maternal sensitivity to distress, and other parenting characteristics, were associated with CU traits over the preschool period, and examined whether this was mediated via infant attachment status.

Method: In an epidemiological cohort, CU traits were assessed at age 2.5, 3.5 and 5.0 years by mother report. Dimensions of parenting were assessed in free play at age 29 weeks in a stratified subsample of 272, and attachment status at 14 months (n = 265). Structural equation modelling with maximum likelihood estimation was used to examine predictions from parenting dimensions and attachment status.

Results: A parenting factor reflecting sensitivity to distress (n = 207), sensitivity to non-distress, positive regard towards the infant, and intrusiveness, predicted child CU traits ($p$ = .023). This effect was accounted for mainly by sensitivity to distress ($p$ = .008) and positive regard ($p$ = .023) which showed a synergistic effect as evidenced by a significant interaction ($p$ = .01). This arose because the combination of low sensitivity to distress and low positive regard created the risk for elevated CU traits. Although sensitivity and positive regard predicted attachment security and disorganization, there were no associations between attachment status and CU traits.

Conclusions: The finding of contributions from both sensitivity to infant distress and positive regard to reduced CU traits suggests that children's responsiveness to others' emotions may be increased by their own mothers' responsiveness to them and their mothers' warmth. There was no evidence that this was mediated via attachment status. Implications for intervention and future directions are discussed.

Keywords: Callous-Unemotional (CU) traits, parenting, infancy, attachment.

## 4.2 Introduction

There is much current interest in a possible subgroup of conduct disordered children who show a lack of concern for the feelings of others and lack of guilt or remorse, labelled as 'callous-unemotional traits' (CU traits) (Frick, 2009). There is some evidence that there may be distinct developmental processes contributing to the development of conduct problems with and without CU traits. Conduct problems in children with CU traits have been found to be more highly heritable (Viding, Jones, Frick, Moffit, & Plomin, 2008), less influenced by negative parenting practices (Pasalich, Dadds, Hawes, & Brennan, 2012) and less responsive to typical conduct problem interventions (Hawes, Price, & Dadds, 2014). CU traits have been linked to more severe and stable antisocial behavior in childhood (Frick, Ray, Thornton, & Kahn, 2014) and of particular interest is the association with physical aggression, with CU traits being associated with more severe violent and aggressive behavior (Kruh, Frick, & Clements, 2005).

Evidence from several prospective general population based studies of children aged two years and older points to the possibility that aspects of positive parenting contributes to lower CU traits. These have included studies of self-reported positive reinforcement and parental involvement (Hawes et al., 2011), parental warmth assessed using the five minute speech sample (FMSS) and observations of parenting in the home (Waller et al., 2014). Using an index of parental sensitivity derived from parent–child observations at ages 24, 36, and 58 months, Wagner et al. (2015) found that less sensitive parenting predicted higher levels of CU traits in first grade controlling for earlier measures of CU behaviors. We have previously reported that maternal sensitivity assessed at age 29 weeks predicted CU traits at 2.5 years (Bedford et al., 2015), and Centifanti, Meins, and Fernyhough (2016) found that mind-mindedness, indexing the mother's awareness of her infant's states of mind, assessed at age 8 months predicted children's self-report of CU traits at 10 years.

As Mesman and Emmen (2013) showed in their meta-analysis, there has been considerable variability in the ways parental sensitivity has been conceptualized and measured. Mary Ainsworth's original coding system focused on the extent of well-timed maternal responses to infant cues, and did not assess maternal warmth, however, subsequent measures have commonly included both in the sensitivity

construct (e.g. Feldman, 1998). Similarly, sensitivity to infant distress and to infant cues while not distressed, may support different infant capabilities and predict different outcomes (Leerkes et al., 2011; McElwain & Booth-LaForce, 2006; Murray et al., 2008). Thus although scores on the dimensions of sensitivity to distress and to non-distress, and of warmth/positive regard, are correlated, assessing their distinctive contributions may be informative in relation to early mechanisms for CU traits. Sensitivity to distress may specifically promote empathy which is a core construct for CU traits (Jones, Happe, Gilbert, Burnett, & Viding, 2010), via processes such as modelling (Kiang, Moreno, & Robinson, 2004) or imitation (Baird et al., 2011). Davidov and Grusec (2006) have previously argued for a specific link between responsiveness to distress and child empathy. In a cross-sectional study of 6-8 year olds, higher maternal sensitivity to distress, but not warmth, was associated with higher child empathy. In a randomized controlled trial of the effect of foster care in children experiencing early institutional deprivation, observed sensitivity to distress, but not warmth, assessed at 30 and 42 months of age, predicted lower CU traits in early adolescence (Humphreys et al., 2015).

The contingent responding to infant gestures characteristic of high sensitivity may contribute specifically to increasing eye contact between infant and parent. This may mitigate the reduced eye contact found in children with CU traits and hence enhance empathic responding (Dadds et al., 2006; Dadds et al., 2014). The finding that a reduced preference for the human face compared to inanimate objects over the human face at 5 weeks of age is associated with CU traits at age 2.5 years (Bedford, Pickles, Sharp, Wright, & Hill, 2015) suggests this may operate early in development (Bedford et al., 2017).

Sensitivity to distress may also be important by virtue of its association with attachment status. A possible role for attachment processes was indicated by the finding in Wagner et al. (2015) that the association between low parental sensitivity and CU traits was mediated in part by scores for dysfunctional family representations derived from children's drawings of their families completed in first grade. Thus empathy, and hence lower CU traits, may be promoted by internalization of the experience of empathic responding by parents. Evidence for the role of attachment status in relation to CU traits comes from a study of 3–9 year olds referred with

conduct problems (Pasalich et al., 2012). Higher CU traits were associated with insecure and with disorganized attachment, based on the Manchester Child Attachment Story Task, a story completion task in which children are asked to portray resolutions of attachment challenges such as being frightened in the night (Green, Stanley, Smith, & Goldwyn, 2000). Willoughby et al. (2014) showed that attachment disorganization assessed at 3 years was associated with a stronger association between the combination of ODD and CU traits and aggression, but did not examine its association with CU traits in multivariate analysis.

Overall the available evidence suggests that aspects of positive parenting in early childhood are associated with lower CU traits, however, little is known about the role of parenting during infancy, and the contributions of specific dimensions of parenting have not previously been examined. Furthermore, the question of whether infant attachment status mediates any associations has not been previously addressed. In this study, we examined specificity of parenting dimensions by comparing contributions from a general parenting factor as well as direct pathways from each separate parenting dimension in SEM. SEM also allowed us to generate a robust indicator of CU traits as the outcome derived from measurement at 2.5, 3.5 and 5.0 years. Based on available evidence we predicted that maternal sensitivity, and not an index of warmth 'positive regard', would be associated with lower CU traits. In view of several lines of evidence that sensitive responding to distress may promote empathy we predicted that the effect of maternal sensitivity would be specific to mothers' responses to distress. We also examined whether the associations between maternal sensitivity and CU traits were mediated via infant attachment status.

## 4.3 Method

### *4.3.1 Sample*

Participants were members of the Wirral Child Health and Development Study, a prospective epidemiological cohort study starting in pregnancy. The cohort consists of 1233 first-time mothers who had live singleton births. Socioeconomic conditions on the Wirral range between the deprived inner city and affluent suburbs, but with very low numbers from ethnic minorities. Mean age of the mothers at

recruitment was 27.9 years (*SD* = 6.2, range 18-51), 42% of the extensive sample were in the most deprived quintile of UK neighborhoods (IMD; Noble et al., 2004) and 96% were White British.

The measures used in this report were obtained for the whole cohort from questionnaires at initial recruitment at 20 weeks gestation and ratings of the child behavior when aged 3.5 years (*M* = 41.89 months, *SD* = 2.5; n = 827) and 5.0 years (*M* = 58.64 months, *SD* = 3.7; n = 775). Additional measures were obtained for a random sub-sample stratified by psycho-social risk of mothers (n = 316) who were to provide interviews at 32 weeks gestation (*M* = 32.1, *SD* = 2.0) and mother–infant observational measures with the child aged 29 weeks (*M* = 29.1 week, *SD* = 3.1; n = 272) and 14 months (*M* = 14.3 months, *SD* = 1.9; n = 268) and additional ratings of the child behavior when aged 2.5 years (*M* = 31.11 months, *SD* = 2.67; n = 253). The stratified sampling has been described in more detail previously (Sharp, Pickles, Meaney, Marshall, Tibu, & Hill, 2012) and analyses included the stratification variable, psychological abuse in the partner relationship (Moffitt et al., 1997), to adjust for effects associated with the relative oversampling of mothers with high psycho-social risk.

The sample analyzed here comprises all participants who provided observational data at age 29 months (n= 272). This subsample was a relatively even mix of boys (n = 134) and girls (n = 138). At age 5.0, 80% of mothers were either married or cohabiting, 5% had a partner living elsewhere and 15% were single.

#### 4.3.2 *Ethical considerations.*

All women gave written informed consent at the point of recruitment in the antenatal clinic. Ethical approval for the study was granted by the Cheshire North and West Research Ethics Committee on the 27th June 2006.

#### *4.3.3 Measures*

*Maternal sensitivity.*

Mother-child interactions at 29 weeks were videotaped during a semi structured 15-min play session in a purpose built room in the study base. Mother–infant dyads played with a toy of the mother's choice for the first 7 minutes and with a standard set of toys provided by the experimenter for the following 8 minutes (as described in National Institute of Child Health and Human Development - Early Childcare and Youth Development [NICHD-ECCRN], 1999). The interactions were coded for maternal sensitivity to non-distress and to distress, positive regard and intrusiveness using the NICHD manual (Owen, 1992). All the parenting codes are rated on a global 5-point scale, ranging from 1 (*not at all characteristic*) to 5 (*highly characteristic*). Sensitivity to distress captured the extent to which the mother responded to her infant's cries, frets or distress in a consistent, timely, and appropriate manner. Sensitivity to non-distress captured the extent to which the mother observed and responded in a well-paced and appropriate manner to her infant's social gestures, expressions, and signals of non-distress. Positive regard captured the parent's positive feelings towards the child expressed during the interaction, shown by behaviors such as smiling at the child or laughing with the child. Intrusiveness captured the extent to which the interaction is adult centered rather than child centered, shown by behaviors such as not allowing the child to handle toys they reach for or insisting that the child do something (play, eat, interact) in which they are not interested. Sensitivity to distress was coded on the 207 of the 272 children who showed distress during the assessment. Training on the sensitivity measure was provided by an investigator from the NICHD Network. Three raters, blind to the other measures, coded sensitivity from video recordings. Each rater achieved good inter-rater reliability for maternal sensitivity, positive regard and intrusiveness on a subset of 30 assessments (ICCs .83-.89). Ratings were log transformed to minimize skew and standardized to aid effect comparison.

*Attachment security.*

Infant–mother attachment was assessed at 14 months using the Strange Situation Paradigm (Ainsworth, Blehar, Waters, & Wall, 1978). The Strange Situation is a widely used laboratory procedure designed to assess the attachment relationship between infants aged 12–20 months and a caregiver. One trained rater who was blind to all other study data coded all infant–mother strange situations, and assigned them as Secure, Avoidant, Resistant or Disorganized. To evaluate inter-rater

reliability, 53 strange situations (20%) were selected randomly for coding by a second trained rater who was also blind to the study details. The two coders achieved inter-rater reliability on the four-way classification (81% exact agreement; kappa = .72) coding schemes. 268 children in total completed the strange situation paradigm, of which 3 were assigned 'cannot classify' and were not included in analyses. In the four-way classification, 128 (48%) of children were secure, 87 (33%) were disorganized, 27 (10%) were avoidant and 23 (9%) were resistant. For this analysis we created two binary variables: secure = 0/insecure = 1 and organized = 0/disorganized = 1.

*CU traits.*

CU traits were assessed by mother-report at 2.5, 2.5 and 5.0 years using a combination of the Antisocial Personality Screening Device (Frick & Hare, 2001) and items from the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2000), the Brief Infant Toddler Assessment (BITSEA; Briggs-Gowan, Carter, Irwin, Wachtel, & Cicchetti, 2004) and the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997). We have previously created CU traits latent factor scores at age 2.5 and 5.0 years (Wright et al., submitted) by subjecting items to exploratory and confirmatory factor analyses in MPlus (Muthen & Muthen, 2012). For this study we applied the same process to the age 3.5 year items (see section 4.7 supplementary material S1). We allowed the items at each age to vary to reflect developmental differences in the manifestation of CU traits, the items for each age are displayed in Table 4.7.1.1. For this analysis, a latent variable was created from the three factor scores to represent CU traits from age 2.5 to 5.0 years.

*Covariates.*

Covariates reflected family demographic status, partner psychological abuse at entry to the study to account for the stratification, maternal mood at times of reporting of CU traits to account for possible mood based reporting biases, and infant fear because of evidence that elevated fear may be a risk for later CU traits (e.g. Waller et al., 2016). Two indices of family demographic status were included as covariates: 1) socio-economic status, which was derived from post code data using the English Index of Multiple Deprivation (IMD) (Noble et al., 2004) and converted to quintile categories with a binary variable (1 = most deprived, 0 = all 4 other

quintiles) used for analysis and 2) mother's age at consent . The stratum variables indicating stratification status created from the partner psychological abuse measure (Moffit et al., 1997) were included as covariates. Mother's depression at time of reporting CU traits was assessed at age 2.5 and 3.5 years using the Edinburgh Postnatal Depression (Cox, Holden & Sagovsky, 1987) and at 5 years with the Centre for Epidemiological Studies Depression Scale (Radloff, 1977) at age 5.0. A standard score was created at each age and a mean score of the three time points was used for analysis. Infant fear at age 29 weeks was assessed using the unpredictable mechanical toy task from the Laboratory Temperament Assessment Battery (Lab-TAB; Gagne, Van Hulle, Aksan, & Essex, 2011). In this task the infant is exposed to an unpredictable mechanical toy for 60 seconds, each 10 second epoch is coded on a 3 point scale for facial, bodily and vocal fear, and escape behaviors, and a mean score across all epochs is used for analysis. Two raters, blind to the other measures, coded the Lab-TAB from video recordings. Acceptable reliability was achieved on a subset of 30 assessments (ICC = .74).

*4.3.4 Analysis plan*

All analyses were conducted in Stata version 14 (Statacorp, 2015). The main analyses used structural equation modelling (SEM) using the *sem* and *gsem* commands, the latter being required for models that included the binary attachment status outcomes, with maximum likelihood estimation. The analyses proceeded by first examining prediction from each NICHD parenting code (sensitivity to distress, sensitivity to non-distress, positive regard, intrusiveness) to attachment status and to child CU traits. Then the four parenting variables were modelled as a general parenting latent variable and prediction using this general parenting factor was examined. If prediction from the factor was shown, further sem models were then estimated with a direct path added from each parenting variable to test for specificity of prediction among the four parenting measures. We then examined the prediction of CU from attachment and the four parenting measures, for the latter following the same procedure as for the prediction of attachment.

Since we wished to make inference about all mothers and infants, and not just those with distressed infants, we needed to include in the analysis all dyads, regardless of distress status. Maximum likelihood modelling of the general parenting

factor also allowed us to tackle this problem of an absence of a measure of sensitivity to distress whenever the infant failed to show distress during the observation, under an assumption of missing-at-random. This allowed the probability of such missingness to be associated with a parent's sensitivity to non-distress, positive regard, and intrusiveness as well as included covariates and stratifiers. To examine each individual contribution of each parenting indicator in turn, the error variance of each indicator was in turn set to zero so that the factor reflected each specific indicator one at a time.

Finally, for the prediction of CU traits, we examined for possible synergy among parenting indicators identified as important. We calculated the product of centered scores from two parenting indicators as an additional indicator of the factor and, as above, examined whether there were additional effects from this product indicator along a direct path to the CU factor.

Model fit using the *sem* command was assessed using the Root Mean Square Error of Approximation (RMSEA) and the Comparative Fit Index (CFI). RMSEA less than .05 and CFI greater than .95 are indicative of good fit~~,~~ whereas RMSEA less than .08 and CFI greater than .90 represent reasonable fit (Hau, Marsh & Wen, 2004). Stata does not produce fit statistics for *gsem* models, so for these models we relied on the size and significance of the estimates alone.

## 4.4 Results

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**Table 4.4.1.1** Summary statistics and bivariate associations (Spearman's rho) between main study variables and covariates

| | CU Factor | Distress | Non-distress | Intrusive | Pos. Regard | Insecure | Disorg. | Infant fear | Mat. Dep. | Risk | Mat. age | Deprived |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sensitivity distress | -.27*** | | | | | | | | | | | |
| Sensitivity non-distress | -.19** | .72*** | | | | | | | | | | |
| Intrusiveness | .09 | -.38*** | -.50*** | | | | | | | | | |
| Positive regard | -25*** | .71*** | .81*** | -.32*** | | | | | | | | |
| Insecure attachment | .07 | -.11 | -.11 | .05 | -.11† | | | | | | | |
| Disorganised attachment | -.01 | -.12 | -.12† | .09 | -.14* | .31*** | | | | | | |
| Infant fearfulness | -.04 | .03 | -.01 | .02 | .01 | -.04 | .09 | | | | | |
| Mothers depression | .17** | -.01 | -.06 | .02 | -.10 | .05 | .04 | .03 | | | | |
| Sample risk stratum | .16** | -.15* | -.16* | .13* | -.12† | .05 | .13* | .01 | .18* | | | |
| Maternal age | -.19*** | .31*** | .39*** | -.20** | .33*** | .01 | -.03 | -.07 | -.06 | -.17** | | |
| Deprived | .09 | -.20*** | -.24*** | .16** | -.23*** | .02 | .09 | -.01 | .02 | .08 | -.31*** | |
| N | 272 | 207 | 272 | 272 | 272 | 265 | 265 | 272 | 271 | 272 | 272 | 272 |
| Mean | -0.01 | 3.42 | 3.70 | 1.89 | 3.60 | 0.62 | 0.33 | 0.41 | -0.01 | 0.76 | 27.78 | 0.38 |
| (SD) | (0.29) | (1.00) | (0.99) | (0.87) | (0.91) | (0.49) | (0.47) | (0.33) | (0.84) | (0.78) | (6.18) | (0.49) |

Note. ***$p < .001$, **$p < .01$, *$p < .05$, †$p < .10$

*4.4.1 Summary statistics*

The simple correlations and summary statistics for all the variables are presented in Table 4.4.1.1. It can be seen that maternal sensitivity to distress, sensitivity to non-distress and positive regard were strongly correlated, with intrusiveness showing weaker but still substantial correlations with the other parenting variables. Lower maternal sensitivity and positive regard, and higher intrusiveness, were associated with being younger at the time of first child, being exposed to partner psychological abuse during pregnancy (sample risk stratifier) and living in an area of high deprivation, underlining the importance of controlling for these variables in all subsequent analyses.

*4.4.2 Parenting to attachment status*

Models predicting binary attachment status used the *gsem* command and produced unstandardized probit coefficients. Examining the effects of each indicator in turn showed that sensitivity to distress was associated with insecure attachment (est = -0.18, 0.01 to 0.36, $p$ = .046), and there were similar but marginal effects for positive regard ($p$ = .068) and to a lesser extent sensitivity to non-distress ($p$ = .104) and non-significant effects in the opposite direction for intrusiveness ($p$ = .424). The factor formed by the four parenting indicators together (with a negative factor loading for intrusiveness), while giving a reasonable model fit (RMSEA = .04, CFI = .99), showed only a marginally significant effect on insecure attachment ($p$ = .079).

Corresponding analyses for disorganized attachment gave an identical pattern of findings, with low sensitivity to distress a significant predictor (est = 0.21, 0.02 to 0.40, $p$ = .024), and similar effects of low positive regard ($p$ = .061), low sensitivity to non-distress ($p$ = .173) and intrusiveness ($p$ = .362). Here again the parenting factor's effect was similar to that of the individual measures and of marginal significance. ($p$ = .083).

*4.4.3 Prediction of CU traits from attachment and parenting*

We fitted a confirmatory factor analysis model to the CU traits measurements at age 2.5, 3.5 and 5.0 year (see appendix S1 for a description of their construction). The model showed good fit (RMSEA = .00, CFI = 1.00) with factor loadings of .69, .80 and .67 for age 2.5, 3.5 and 5.0 years respectively.

Models for the prediction of CU traits by attachment status fit well but, as shown in Figure 4.4.3.1, neither insecure nor disorganized attachment made independent contributions (secure: $p$ = .265; organized: $p$ = .652). Figure 4.4.3.2 shows the results from the models considering each of the parenting indicators as predictors of CU traits in turn. Sensitivity to distress (β = - .20, -.34 to -.05, $p$ = .008) and positive regard (β = - .18, -.33 to -.03, $p$ = .023) were associated with lower CU traits, and there was a similar but non-significant effect of sensitivity to non-distress (β = - .13, -.27 to .02, $p$ = .088). The effect of intrusiveness was much smaller and non-significant (β = -.05, -.19 to .08, $p$ = .461).

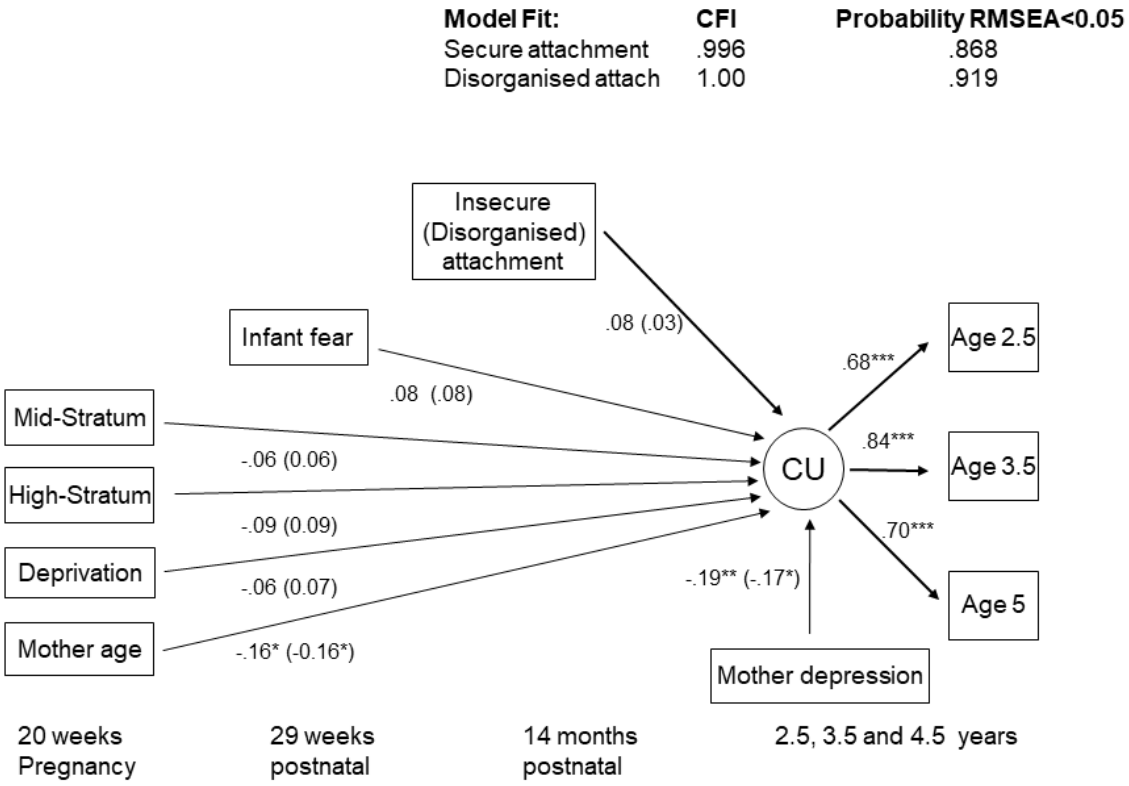


*Figure 4.4.3.1.* Standardized estimates for insecure attachment model and disorganized attachment model (in parentheses) predicting child CU traits. Note. *p<.05 **p<.01 ***p<.001

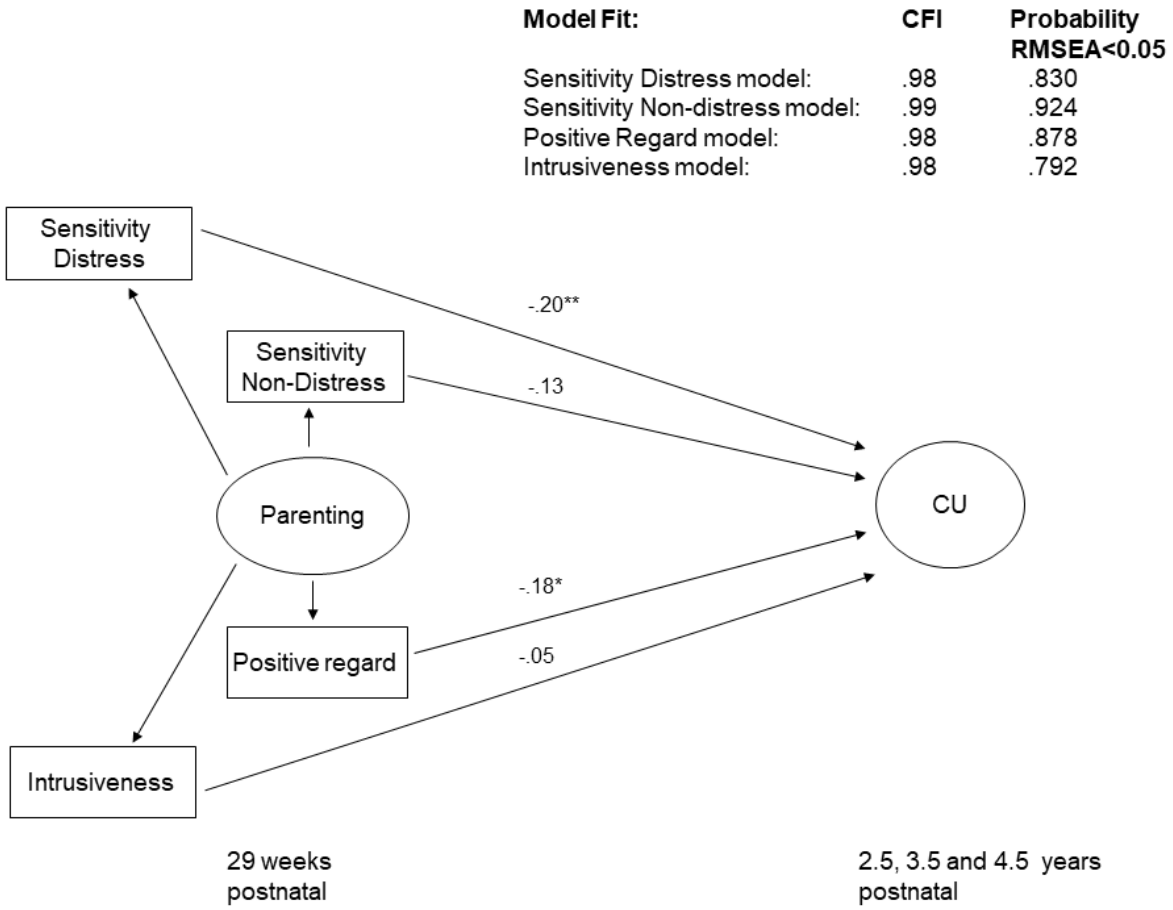


*Figure 4.4.2.* Standardized estimates for each parenting indicator predicting child CU traits. Note. *p<.05 **p<.01 ***p<.001. This figure depicts the results of four separate sem models.

The general positive parenting factor formed by the four indicators together significantly predicted lower CU traits (β = -.18, -.33 to -.03, *p* = .023) explaining 13% of the variation in the CU factor. This model, shown in Figure 4.4.3.3, was then extended in two ways to clarify the prediction of CU traits. The first examined whether any aspects of parenting showed a particular association with CU traits beyond that implied by their contribution to the general parent factor, by testing for the effect of including the specific pathway from each parenting variable on the CU traits factor. The addition of either the sensitivity to distress or positive regard direct pathways rendered the effect of the parenting factor non-significant, suggesting that each contributed substantially to the effect of the factor. When added to the effect via the parenting factor, the direct pathway was significant for positive regard (*p* = .036),

but not the sensitivity to distress ($p$ = .165). Addition of the intrusiveness and sensitivity to non-distress pathways had little impact on the prediction from the parenting factor to CU traits, indicating that they did not make major contributions to its effect on CU traits, though the estimates for the latter model showed collinearity problems.

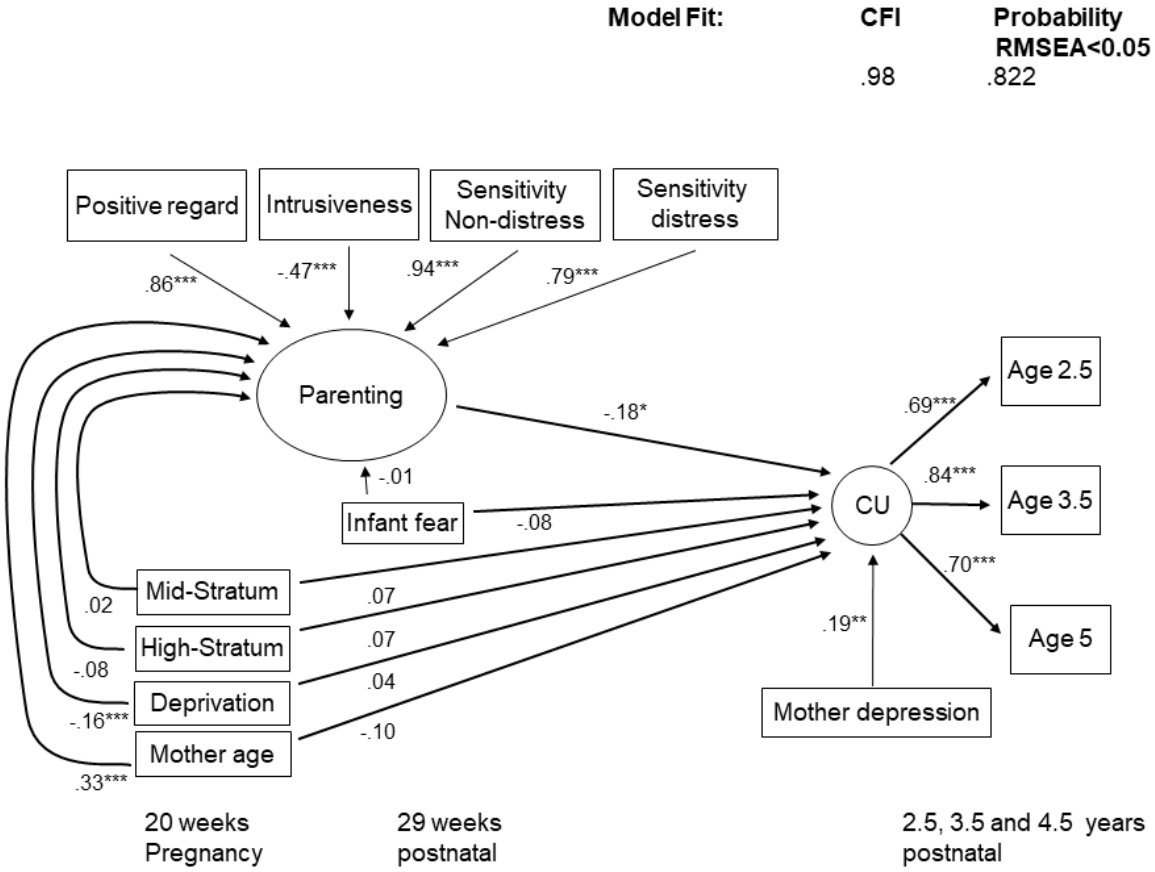


*Figure 4.4.3.3.* Standardized estimates for the latent parenting factor predicting child CU traits. Note. *p<.05 **p<.01 ***p<.001

As analyses of the parenting indicators separately, and in relation to the parenting factor, had indicated roles for sensitivity to distress and positive regard, we examined whether they had a synergistic effect by including an additional indicator formed by the interaction between sensitivity to distress and positive regard. The additional path from the interaction term to the CU factor was significant ($p$ = .010; Model fit: RMSEA = .05, CFI = .96), and raised the explained variance of the CU

factor to 17%. The effect of the interaction is shown in Figure 4.4.3.4 contrasting effects of sensitivity to distress in groups below and above mean positive regard. It can be seen that high CU traits were predicted by the combination of low positive regard and low sensitivity to distress, but not by either one of these in the absence of the other. A final check showed that this interaction had no role in the prediction of secure or organized attachment.

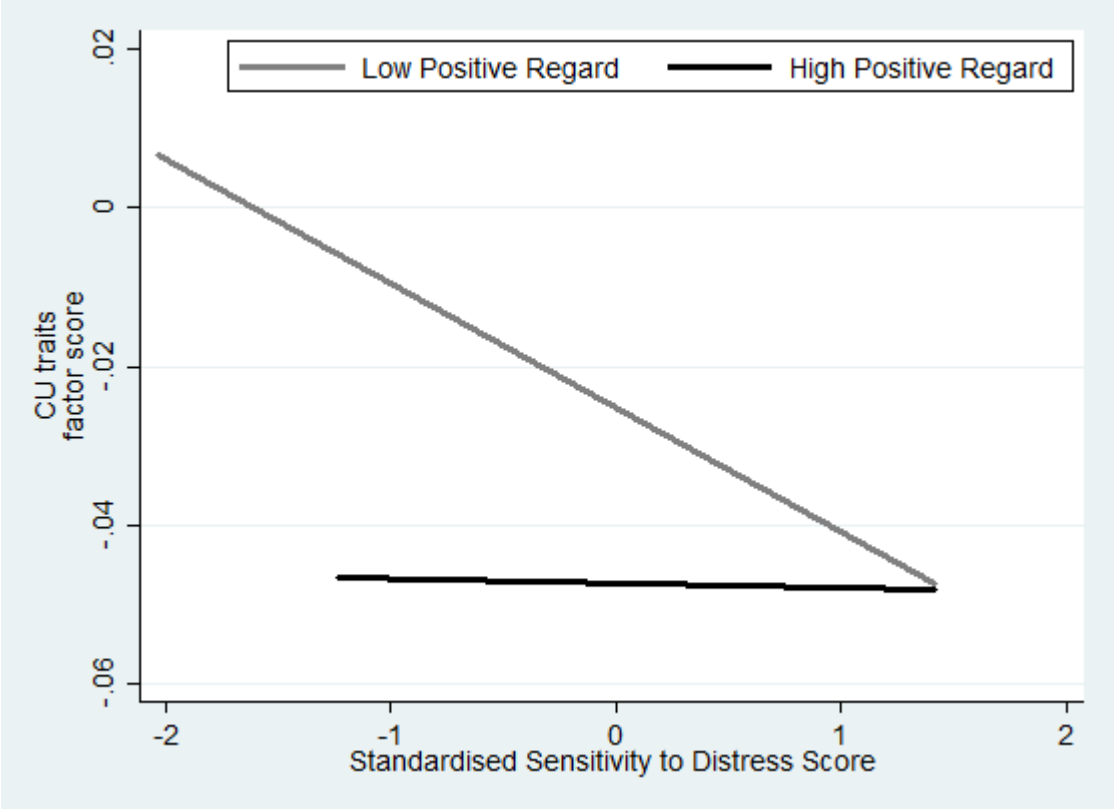


*Figure 4.4.4* Plot showing prediction of CU traits from sensitivity to distress at high and low positive regard groups, divided at the mean score.

## 4.5 Discussion

In a longitudinal general population sample with observed maternal behaviors at age 29 weeks, assessment of attachment security in the Strange Situation at age 14 months, and maternal reports of CU traits at age 2.5, 3.5 and 5.0 years, we showed that increased positive parenting reflecting both maternal sensitivity and maternal

positive regard in infancy were associated with reduced CU traits in early childhood. Sensitivity to distress and positive regard clearly had stronger effects than either sensitivity to non-distress or intrusiveness, and they acted synergistically so that the risk for high CU traits arose from the combination of low sensitivity to distress and low positive regard. Although maternal sensitivity to distress predicted attachment security and disorganization, neither was associated with subsequent CU traits, thus providing no evidence for mediation of the effect by attachment status at 14 months. This is the first study to provide support for a specific role for two facets of positive parenting during infancy, sensitivity to distress and positive regard, in relation to CU traits over the preschool period, and to show that attachment security is not implicated in these early processes.

The findings are consistent with work with older children suggesting that parental responsiveness to distress may play a role in child empathy development (Davidov & Grusec, 2000; Humphreys et al., 2015). The findings are also consistent with the broader literature documenting associations between positive aspects of parenting and CU traits from the preschool period through to late childhood (e.g. Waller et al., 2014; Hawes et al., 2011). However, contrary to our predictions, sensitivity to distress was not unequivocally the strongest predictor of CU traits, and on balance maternal positive regard, irrespective of the infant's emotional state, may have been the stronger predictor. The finding of a significant interaction between sensitivity to distress and positive regard suggested that the risk for CU traits arises from a combination of lack of contingent responding to distress and lack of warmth. This needs replication, but the implication for intervention studies is that improvements in either parenting characteristic would be associated with lower CU traits.

In line with previous findings, lower maternal sensitivity to distress was significantly modestly associated with insecure attachment, with sensitivity to non-distress a non-significant predictor (McLewian & Booth-LaForce, 2006; Leerkes et al., 2011). The same pattern of findings was true for disorganized attachment status. Neither insecure nor disorganized attachment at 14 months predicted later CU traits. In spite of the many differences in samples and measures between this study and the study of Pasalich et al (2012), the contrast in findings may indicate that attachment

status contributes to CU traits specifically in the context of conduct problems, or environmental risks associated with conduct problems. Alternatively, consistent with findings reported by Wagner et al. (2015) and Pasalich et al., attachment processes may contribute to risk of CU traits only after infancy. In order to maintain comparability with most other studies of attachment and externalizing problems we did not examine associations with dimensional indices of attachment. Given the evidence that attachment categories are not natural taxon's (Fraley & Spieker, 2003), a dimensional approach may have given a different result. It seemed therefore that the association between higher maternal sensitivity to distress and reduced CU traits was not mediated via attachment status, suggesting that there may be at least two pathways from maternal sensitivity to later developmental outcomes. One, mediated via attachment security may be specific to emotion regulation with a caregiver, while the other may entail the promotion of emotional and social understanding and responsiveness more generally.

The study was characterized by a number of strengths in the study design, sample and measurement. This was a prospective study of a consecutive sample from an antenatal clinic serving a defined geographical area. Sequential measurement of maternal parenting characteristics, infant attachment status and child CU traits made it possible to conduct mediation analyses. We used several indicators of parenting, examining both their joint effect as a factor, and their additional independent effects, and their interaction. Parenting characteristics and infant attachment ratings were based on observations, and independent ratings were made blind to each other and to other measures. The problem of selection of sensitivity to distress measures by infant distress was addressed by using a latent variable approach with the pattern of relatedness observed in dyads with all four parenting variables present used to predict the missing data on sensitivity to distress. We followed an approach previously used to combat low internal consistency in CU traits measures (Dadds et al., 2005) by using exploratory and confirmatory factor analysis on a widely used measure, the APSD, and other relevant developmentally appropriate items from early childhood problem behavior measures. This created measures with acceptable psychometric properties. Finally, we took a latent variable approach to modelling the CU traits outcome by combining reports from three time points throughout early childhood. This increased the robustness of the results by reducing the influence of measurement

error. It also allowed us to examine a CU traits outcome that reflected persistence of CU traits, likely to be associated with poorer outcomes later in childhood.

Limitations of the study include that CU traits were assessed using mother-report only. We sought to account for the effects of maternal mood on reporting, but could not rule out that mothers who are themselves less sensitive to distress may perceive their children as being less empathic. We also cannot exclude common genetic influences on maternal sensitivity and children's CU traits. The sample is almost exclusively White British so the findings may not be not generalizable to other ethnic groups. Finally, both sensitivity to distress and to non-distress were coded from the same free-play task and it is possible that distress occurring during a playful context may not be representative of maternal responses to distress in more threatening situations (Leerkes, 2011).

We have identified a possible specific mechanism involved in the early emergence of CU traits which may serve as a potential target for intervention, with the prospect that the relevant outcomes can be identified relatively soon after the intervention. We measured sensitivity at 29 weeks, however, maternal sensitivity measured even earlier has been linked to poorer child outcomes in other studies (e.g. 2 months; Hentges et al., 2011) which makes the case for examination of parent-infant interaction and later outcomes with measurements at multiple points over the first year of life. Previous work has indicated that infants who show low eye gaze early in development may be an important target group for study and hence intervention, an important avenue for future work should focus on studying the interplay between maternal parenting characteristics and low eye gaze in samples of heightened risk across early development.

## 4.6 Conclusion

In sum, the current study provides further evidence that aspects of positive parenting are associated with reduced child CU traits. The findings are the first to indicate a specific role for maternal sensitivity to distress, and to show that attachment security or disorganization do not mediate this association. The findings

have implications for research examining early developmental pathways to CU traits and for potential preventative intervention.

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## 4.7 Appendix S1: Creation of the age 3.5 years CU traits factor score

### *4.7.1 Rationale*

Existing measures of CU traits were developed and validated with samples of children of mid to late childhood age. The majority of studies of children under 5 years of age have created hybrid measures of CU traits from other child problem behaviour measures. These scales have tended to comprise a small number of items and thus suffer from low internal consistency reliability. Dadds, Hawes, Frost, and Fraser (2005) supplemented the Antisocial Personality Screening Device (APSD; Frick & Hare, 2001) a widely used measure of CU traits in older samples, with the prosocial items from the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) to improve the internal consistency of the measure. We have taken the same approach by supplementing the APSD with items from a number of child problem behaviour measures. We sought to establish a measure that is invariant across sex to allow the measure to be used to test for sex differences in associations between CU traits and other variables of interest.

### *4.7.2 Method*

Following the approach used in Wright et al. (submitted) items from three different child problem behaviour measures were subjected to exploratory and confirmatory factor analyses. All six items from the CU subscale of the APSD were selected. Six items were selected from the Child Behaviour Checklist (CBCL; Achenbach & Rescorla, 2000) the item ‘doesn’t seem to feel guilty after misbehaving’ was not included due to similarity to the APSD item ‘feels bad or guilty when he/she does something wrong’. Finally, one item from the Brief Infant Toddler Socio-emotional Assessment (BITSEA; Briggs-Gowan, Carter, Irwin, Wachtel & Cicchetti, 2004) was included based on its similarity to the SDQ prosocial items. All items are rated on a three point scale (0, 1, 2). The same 13 items were considered for age 2.5 in Wright et al., 17 items were considered for age 5 as the SDQ prosocial items were available at that age. Also following on from the approach taken in Wright et al. we used 5 physical aggression items taken from the work of Baillargeon et al. (2007) to examine whether parents were reliably able to distinguish CU items from aggression items. All the items used are displayed in Table 4.7.2.1.

In the first stage of the analysis, the CU items were entered into an exploratory factor analysis for ordinal data (using the weighted least squares mean adjusted estimator [WLSM] and promax rotation) in Mplus version 7 (Muthen & Muthen, 2012). Items with a factor loading >.35 were retained. A series of multi-group two-factor CFA models were then used to examine for measurement invariance across sex in CU traits and aggression. The weighted least squares means and variance adjusted (WLSMV) estimator and Theta parameterization were used. In model 1 (configural model) the pattern of factor loadings were constrained to be the same for boys and girls, testing that the same items form the CU and aggression factors across sex. In model 2 (metric model) the individual factor loadings were constrained to be the same, testing whether the contribution of individual items varies by sex (weak factorial invariance). In model 3 (scaler model) the thresholds were also constrained to be the same, to examine whether the items perform the same across sex (strong factorial invariance). Full invariance is demonstrated when placing additional constraints on the model does not produce a significant worsening in model fit. The *DIFFTEST* command was used to evaluate whether a substantial change in model fit occurred as a result of imposing additional constraints, as well as the CFI change (ΔCFI). A non-significant chi-square difference test and a small CFI change (in which a decrease is no greater than .01) are considered indicative of invariance (Cheung & Rensvold, 2002). If a significant chi-square difference test is found, the modification indices are examined to determine which items failed the strong factorial variance assumption. In the absence of modification indices the individual items are checked for those showing the largest difference between boys and girls. The thresholds of these items are then allowed to vary freely and model fit is re-examined as a test of partial strong factorial invariance. Further, the modification indices are inspected for each model to check for cross-loading of CU items on the aggression factor. Items which fail the factorial invariance assumption or items with modification indices that indicate cross-loading will be evaluated for removal from the model.

CFA was then used to compare a two-factor CU and aggression model to a model where all CU and aggression items loaded on the same factor, to test whether parents could reliably distinguish CU traits items from aggression items. The two models were compared using the DIFFTEST command.

To avoid numerical problems associated with sparse data, where endorsement rates were < 1.5%, scores of 1 and 2 were collapsed to create binary variables. This was applied to the CU traits items 'cruel to animals', 'shows little affection' and unresponsive to affection' and all of the aggression items. Although this generated adequate cell sizes in the sample as a whole, the analytic approach required adequate numbers in both males and females. Following the approach taken in Wright et al. 'gets in many fights" was combined with the similar item "physically attacks others", and "bites other children" was combined with the next rarest item "kicks other children".

### *4.7.3 Results*

*Exploratory factor analysis on the age 3.5 CU items***.** The 13 CU items were entered into an EFA. Eigenvalues for first three factors were 4.8, 1.5, and 1.2, and the scree plot supported a one factor solution. All items gave factor loadings >.35 and so all items were retained.

*Confirmatory factor analyses testing measurement invariance.* The 13 CU items and the three aggression items were then tested for measurement invariance across sex. Model 1, the configural model, showed acceptable fit (RMSEA = .06, CFI = .91). However, the modification indices indicated that items 'CBCL: cruel to animals' should cross-load on the aggression factor for girls and 'CBCL: selfish' should cross-load on aggression for boys. These items were removed and a further configural model (Model 1b) was tested on the remaining 11 items and showed improved fit (RMSEA = .05, CFI = .96) with no further modification indices. The introduction of factor loading invariance with model 2 resulted in a very slight improvement in fit (RMSEA = .04, CFI = .96). However, the chi-square difference test was significant ($p$ = .034) and inspection of the modification indices suggested that item 'APSD: does not show feelings or emotions' should load positively on the CU factor for boys and negatively for girls. In our previous analyses on the 5 year data this item did not show a factor loading >.35 in the initial EFA, and other studies have similarly not found this item to load sufficiently with the other APSD items (Dadds et al., 2005). Therefore we ran a third configural model (Model 1c) with this item removed. This model showed good, but not improved fit (RMSEA = .05, CFI = .96) and modification indices now indicated that item 'BITSEA: tries to help others' should

cross-load on aggression. This item was removed, and a further configural model (Model 1d) was tested on the remaining 9 items. This model showed very good fit to the data (RMSEA = .01, CFI = 1.00) and presented no further modification indices. Factor loading invariance was then introduced with Model 2b, this model showed good fit (RMSEA = .02, CFI = 1.00) and a non-significant chi-square difference test indicated that imposing factor loading invariance did not significantly worsen the fit of the model (p = .245). The introduction of threshold invariance in Model 3 resulted in a slight improvement in fit (RMSEA = .01, CFI = 1.00) and the chi-square difference tests' were non-significant for the comparison to Model 1d ($p$ = .345) and Model 2b ($p$ = .901). Therefore strong factorial invariance across sex was achieved on the remaining 9 items. The full model fit and comparison results are presented in Table 4.7.3.1.

**Table 4.7.2.1** Standardised factor loadings from the CU and aggression CFA for ages 2.5 years, 3.5 years and 5 years

| Items | Age 2.5 | Age 3.5 | Age 5 |
|---|---|---|---|
| **CU traits items** | | | |
| APSD 1: Concerned about the feelings of others (R) | .48 | .42 | .41 |
| APSD 2: Seems motivated to do his/her best in structured activities (R) | .61 | .37 | |
| APSD 3: Is good at keeping promises (R) | .54 | .51 | .49 |
| APSD 4: Feels bad or guilty when he/she does something wrong (R) | .48 | .46 | .61 |
| APSD 5: Keeps the same friends (R) | .36 | .16 | .49 |
| APSD 6: Does not show emotions | | | |
| CBCL 14. Cruel to animals | .93 | | .59 |
| CBCL 58: Punishment doesn't change his/her behavior | .62 | .74 | .68 |
| CBCL 67: Seems unresponsive to affection | .77 | .69 | .81 |
| CBCL 69: Selfish or won't share | .42 | | |
| CBCL 70: Shows little affection toward people | .48 | .75 | .82 |
| CBCL 72: Shows too little fear of getting hurt | | .49 | |
| BITSEA 22. Tries to help if someone is hurt (R) | .69 | | |
| SDQ 1: Considerate of other people's feelings (R) | | | .82 |
| SDQ 4: Shares readily with other children (R) | | | .60 |
| SDQ 9: Helpful if someone is hurt, upset or feelings ill (R) | | | .75 |
| SDQ 17: Kind to younger children (R) | | | .70 |
| SDQ 20: Often volunteers to help others (R) | | | .56 |
| **Aggression items** | | | |
| Hits other children | .76 | .89 | .94 |
| Bites other children/Kicks other children | .75 | .84 | .96 |
| Gets in many fights/Physically attacks others | .87 | .88 | .87 |

Note: *APSD = Antisocial Personality Screening Device, BITSEA = Brief Infant Toddler Social and Emotional Assessment, SDQ = Strengths and Difficulties Questionnaire*

**Table 4.7.3.1:** Age 3.5 years CFA models testing measurement invariance across sex

| | **Parameters** | **Chi2(df)** | **p** | **RMSEA** | **RMSEA 90% C. I** | **CFI** |
|---|---|---|---|---|---|---|
| Model 1a: configural | 147 | 386.05(147) | .001 | .06 | .06 - .07 | .91 |
| Model 1b: configural (modified) | 119 | 204.74(111) | .001 | .05 | .04 - .06 | .96 |
| Model 1c: Configural (modified) | 103 | 179.29(97) | .001 | .05 | .04 - .06 | .96 |
| Model 1d: Configural (modified) | 97 | 80.45(75) | .313 | .01 | .01 - .03 | 1.00 |
| Model 2a: metric | 105 | 217.67(125) | .001 | .04 | .03 - .05 | .96 |
| Metric 2b: (modified) | 85 | 95.74(87) | .001 | .02 | .01 - .03 | 1.00 |
| Model 3: scalar | 70 | 108.93(102) | .301 | .01 | .01 - .03 | 1.00 |
| **Model 1b vs Model 2a** | | 25.11(14) | .034 | | | |
| **Model 1d vs Model 2b** | | 14.95(12) | .245 | | | |
| **Model 1d vs Model 3** | | 29.33(27) | .345 | | | |
| **Model 2b vs Model 3b** | | 8.54(15) | .901 | | | |

*One- versus two-factor CFA models.* We then examined whether mothers' could differentiate CU traits and aggression by comparing a one-factor CFA model where all the CU and aggression items loaded on one factor, to the two factor model, using the chi-square DIFFTEST. The model fit statistics and model comparison results are displayed in Table 4.7.3.2 The two-factor model showed the best fit (RMSEA = .01, CFI = 1.00) and the chi-square difference tests indicated that the two-factor model showed significantly better fit (p<.001). The standardised factor loadings are displayed in Table 4.7.3.1.

**Table 4.7.3.2** Comparison of the two-factor CU traits and aggression model to a one-factor model where all items load on the same factor

| | **χ2 (df)** | **CFI** | **RMSEA** | **RMSEA C I** | **Chi2 diff test** |
|---|---|---|---|---|---|
| **Age 3.5 years** | | | | | |
| 1 factor | 116.75 (57)*** | .96 | .05 | .04 - .06 | |
| 2 factor CU traits and aggression | 42.52(56)* | .1.00 | .01 | .00 - .03 | 30.183(1)*** |

****p < .001, *p < .05*

*Descriptive statistics for the age 2.5, 3.5 and 5 years CU traits measures.* Extracted factor scores were used for analysis but an item mean score for each age point was created to produce meaningful means and standard deviations, presented in Table 4.7.3.3. Table 4.7.3.3 shows the spearmans correlations between the item mean scores for the three age points and Table 4.7.3.4 shows the pearsons correlations between the factor scores.

**Table 4.7.3.3** Summary statistics and spearmans correlations between the age 2.5, 3.5, and 5.0 years CU traits item mean scores

| | Age 2.5 CU traits | Age 3.5 CU traits | Age 5.0 CU traits |
|---|---|---|---|
| Age 2.5 CU item mean score | 1.00 | | |
| Age 3.5 CU traits item mean score | .51*** | 1.00 | |
| Age 5 CU traits item mean score | .44*** | .54*** | 1.00 |
| Mean | .41 | .44 | .30 |
| SD | .25 | .27 | .24 |

Note. ****p <.001*

**Table 4.7.3.4** Pearsons correlations between the age 2.5, 3.5, and 5.0 years CU traits factor scores

| | Age 2.5 CU traits | Age 3.5 CU traits | Age 5.0 CU traits |
|---|---|---|---|
| Age 2.5 CU factor score | 1.00 | | |
| Age 3.5 CU traits factor score | .58*** | 1.00 | |
| Age 5 CU traits factor score | .50*** | .59*** | 1.00 |

Note. ****p <.001*

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# Chapter 5: What are the mechanisms for the translation of CU traits to aggressive behaviour? The role of cortisol reactivity in boys[3]

[3] This paper is currently in preparation as Wright, N., Pickles, A., & Hill, J, & Sharp, H. The role of cortisol reactivity in the translation of CU traits to aggression: evidence for sex specific pathways

## 5.1 Abstract

**Background**

Little is known about how callous-unemotional (CU) traits are translated into aggression, and the evidence regarding links between cortisol reactivity and externalising behaviour are inconsistent. Dysregulated hypothalamic-pituitary-adrenal (HPA) axis functioning may be one mechanism through which CU traits translate to aggressive behaviour, and preliminary evidence suggests that this may be sex-specific. We test this hypothesis longitudinally in a community sample of school age children.

**Methods**

Participants were members of a stratified subsample within an epidemiological longitudinal cohort (Wirral Child Health and Development Study; WCHADS) assessed at 5 years and 7 years (n = 283). Cortisol reactivity was assessed at 5 years with exposure to a social stressor, hearing an argument between adults in the next room. CU traits were assessed via mother report at 5 years, and physical aggression via mother report at age 5 years and teacher and mother report at age 7 years.

**Results**

CU traits at age 5 years were significantly associated with aggression at 7 years; there were no bivariate associations between cortisol reactivity and CU traits or aggression. There was a 3 way interaction between sex of child, CU traits and cortisol reactivity ($p = .043$) predicting aggression. Moderation by sex arose because in girls there was an association between CU traits and aggression that was similar at all levels of cortisol reactivity, while in boys the association was markedly different at low and high levels (two way interaction $p < .001$). CU traits at age 5 years strongly predicted aggression age 7 aggression at cortisol reactivity 1 SD below the mean ($p < .001$) but at 1 SD above there was no association ($p = .296$).

**Conclusions**

These longitudinal findings suggest that aggression associated with CU traits in childhood may arise via failure of inhibitory processes, evidenced in lower cortisol reactivity in boys. The implications of the findings and future directions are discussed.

## 5.2. Introduction

The causes of sex differences in child and adolescent psychopathology, whereby boys are more likely to exhibit early onset externalising disorders, and girls' adolescent onset of internalising disorders, remain unclear. One persuasive explanation for the excess of externalising disorders in boys is that the mechanisms are the same in boys and girls but boys are exposed to higher levels of risk (1). However, given the complex combinations of factors that contribute to externalising disorders (2), this does not exclude an alternative possibility, that some risks operate in different ways in boys and girls. This may be true for example in the case of prenatal influences. Links between prenatal risks such as maternal anxiety, depression, life events, and levels of the stress hormone cortisol, and later emotional and behavioural problems in children have been reported (3-7), many with sex specific effects (4, 8-11). Furthermore there is substantial human and animal evidence for sex differences in vulnerability to foetal insults, and for different effects of stress on male and female foetuses (12). Many of the differences in health and behavioural outcomes have been linked to differences in Hypothalamo-Pituitary-Adrenal (HPA) axis mechanisms (13-15). Previous publications from our group and others have suggested that risks associated with maternal HPA axis variations may have opposite effects on male and female foetuses (16-19) with prenatal risks associated with lower physiological and emotional reactivity in boys, but with higher reactivity in girls.

These opposite effects might indicate that either males or females are resilient in relation to the risks, or that there are different kinds of vulnerabilities in males and females. Neurobiological models of the development of antisocial behaviour have proposed a reduced physiological arousal pathway arising from failures to inhibit antisocial beheaviour (20) or by increasing sensation seeking (21). However, an increasing evidence base now suggests that this may be true for males only. Recent studies of autonomic nervous system response to stress are relevant here. Studies of vagal reactivity (assessed as respiratory sinus arrhythmia (RSA) reduction to a stressor) and child externalising symptoms are consistent with vulnerability associated with lower reactivity in boys and with higher reactivity in girls. For example, in one study elevated externalising symptoms were associated with lower

vagal reactivity during a frustration task in boys but with elevated vagal reactivity in girls (22). In another study, exuberant temperament was predictive of externalizing symptoms in girls only when they showed supressed RSA at 24 and 42 months, and in boys only when they showed augmented RSA at 24 months (23). Similarly we have recently reported that higher vagal reactivity to a stressor at 29 weeks of age predicts decreasing oppositional defiant disorder (ODD) symptoms in boys, but increasing ODD symptoms in girls, assessed over the period 2.5 to 5 years (24).

Similar sex differences may also occur in relation to HPA axis reactivity and externalising symptoms. Although a meta-analyses of the relationship between the HPA axis functioning and externalising symptoms in children concluded that there was no overall association with cortisol reactivity (25) several studies published since then suggest that negative findings may have been explained, at least in part, by opposite effects in males and females. The studies, of children between the ages of 6 and 15 years, reported significant moderation by child sex of associations between externalising symptoms and cortisol levels, all of which arose either because externalising symptoms were associated with lower cortisol only in boys, or with higher cortisol only in girls (26-29).

The majority of studies of autonomic and HPA axis functioning have examined contributions to externalising problems. However, biological mechanisms may vary within this broad phenotype. Biological mechanisms in the narrower phenotype characterised by callous-unemotional traits (CU traits) have been identified, notably reduced amygdala responsiveness (30), reduced heart rate reactivity (31), attenuated blink startle response (32), reduced cortisol reactivity in males (33), and low basal cortisol in males not females (34). These findings are consistent with the hypothesis that CU traits predispose to aggression because of failures of violence inhibition associated with impaired amygdala responsiveness and reduced physiological arousal.

Early studies of CU traits in clinical samples did not include non-aggressive children with CU traits, but with the publication of findings from general population studies it has become clear that the size of the association between CU traits and aggression is modest. It seems therefore that, while CU traits create a vulnerability to

aggression, further processes are involved in the translation of CU traits into aggressive behaviours. This is a topic that so far has received limited attention. Studies examining moderators of the link between CU traits or psychopathic traits and aggression have implicated neighbourhood income (35) and attachment-related mentalisation (36). However candidate biological moderators have not previously been examined. Based on current models implicating low physiological arousal in externalising problems, one plausible possibility is that aggression arises from the combined effects of low amygdala responsiveness and low arousal. This would lead to the prediction that low cortisol reactivity will increase the likelihood of aggression in the presence of CU traits. In the light of the evidence for sex differences in vagal reactivity and HPA axis functioning in relation to externalising behaviour problems, this mechanism may be specific to males.

In this study, we test whether cortisol reactivity moderates the relationship between CU traits and physical aggression, and whether this varies by child sex, in a longitudinal community-based sample of children. Cortisol reactivity to a social stressor (overhearing an argument between adults) and mother-reported CU traits were measured at age 5 years. Physical aggression was assessed at age 5 years by mother report and at age 7 years via mother and teacher report.

## 5.3 Method

### *5.3.1 Sample*

Participants were mothers and children taking part in the Wirral Child Health and Development Study (WCHADS), a prospective epidemiological cohort study starting in pregnancy and designed to investigate the earliest origins of childhood conduct problems. All women gave written informed consent at the point of recruitment in the antenatal clinic. The study used a two stage stratified design in which a consecutive general population sample (the ‘extensive’ sample) is used to generate a smaller ‘intensive’ sample stratified by psychosocial risk with more

detailed measurement over time and both are followed in tandem (37). Mother's responses to a questionnaire at 20 weeks of pregnancy (recruitment) assessing psychological abuse in their current or recent partner relationship (38) were used to generate the stratified intensive sample of mothers for more detailed study. The stratification variable was chosen for its known association with a variety of risk factors for early child development.

The whole cohort (extensive sample) comprised 1,233 women of mean age at recruitment of 26.8 years (SD = 5.8, range 18-51) and 41.8% of the sample were in the most deprived quintile of UK neighbourhoods (39). There were 316 mothers recruited to the intensive sample at 32 weeks pregnancy. At age 5 another stratification strategy was employed to increase the numbers of children in the intensive sample at risk for emotional and behavioural problems. This stratification used scores from the Child Behaviour Checklist (CBCL; 40) and the Antisocial Process Screening Device (APSD; 41) from the age 3.5 assessment wave. All children not already in the intensive sample at that point, who completed the age 3.5 home assessment (n = 570) and who scored above the borderline threshold (T score > 60) on the CBCL externalising or internalising problems subscales or above the cut off of 7 on the APSD (42) were eligible and approached for consent to join the intensive sub-sample at age 5. A total of 94 extra children (16.5%) were eligible to join, and of these 75 (79.8%) agreed and completed the age 5 assessment as part of the intensive sample. This process yielded a full intensive sample of 330 with full data from the age 5 lab assessment, of whom 314 (90%) provided complete cortisol data at that visit. 8 cases were subsequently excluded; 5 were found to have supra-physiological levels of cortisol on assay and 3 had given contaminated saliva samples by eating or drinking prior to the final sample being taken.

In the analyses that follow, data from the larger extensive sample successfully followed up to age 7 (n = 778) were used to first estimate the aggression latent variable outcome variable. The main hypothesis driven analyses then use data from the intensive sample comprising 283 cases who provided full data at both age 5 and 7 years. The mean age of this sample at the 5 assessment was 57.59 months (SD = 2.44, range 54 - 69) and at the age 7 assessment was 88.19 months (SD = 3.75, range = 83 - 107) with slightly more boys (n = 145) than girls (n = 138).

*5.3.2 Procedures and Measures*

*Age 5 Procedures and Measures.* A stress induction task was embedded within a 2.5 hour lab assessment. Baseline salivary cortisol samples were taken after consent (approximately 20 minutes after arrival in the lab) and again 20 minutes later. The child was exposed to the stress induction paradigm followed by an emotionally neutral computerised spatial working memory task, with a post-stress cortisol sample taken 20 minutes after onset of the stressor (the intense argument segment of the recording). Participants were instructed not to eat for 30 minutes before the first saliva sample was taken and the researcher ensured that the child had been awake for at least 30 minutes. Mothers completed questionnaires during the child assessment, and families were recompensed for their time with high street shopping vouchers.

*Stress induction paradigm.* The stress paradigm involved the child overhearing an audiotaped recording of an argument between two adults. This task is considered a mild social stressor that successfully elicits significant variability in physiological stress responses (43). Mothers were asked to wait behind a screen whilst the child remained in the lab with the researcher completing the Kiddie Connors Continuous Performance Task (44). The recorded conversation started playing 15 seconds into the task, after a few seconds the researcher informed the child that the sound was people speaking in the next room, the researcher then sat away from the child and busied themselves with paperwork for the remainder of the recording. The seven minute recording comprised two minutes in which two work colleagues could be heard chatting about benign topics, two minutes disagreement, two minutes intense argument, two minutes unresolved anger and one minute resolution.

*Salivary hormone assessment and enzyme immunoassay procedure***.** Salivary cortisol is a well-established sampling method that avoids the stress inducing effects of blood sampling via venepuncture. Salivary cortisol was collected using cotton eye swabs; the swab was placed in the child's cheek by the researcher until it was fully wet. Three swabs were collected and placed in a Salametrics tube. Saliva samples were frozen and stored at -20 degrees C until analysis. After thawing, salivettes were centrifuged at 3,000 rpm for 5 min, which resulted in a clear supernatant of low viscosity. Salivary concentrations were measured using commercially available

chemiluminescence immunoassay with high sensitivity (IBL International, Hamburg, Germany). Sample and reagent handling was semi-automated using a liquid handling robot (Genesis, Tecan, Switzerland) and quality control samples of low, medium, and high cortisol concentrations were run on each microtiter plate assayed. The intra and interassay coefficients for cortisol were both below 8%. The derived cortisol scores were winsorized and cortisol reactivity was assessed by calculating a difference score between the mean of the two baseline cortisol samples and the post-stressor sample.

Cortisol levels vary throughout the course of the day, however, as this investigation was part of a large scale ongoing longitudinal study it was unrealistic to conduct the assessments at the same time of day for all participants. Time of first cortisol sample was at average 11:58 (SD 2:11 hours) and ranged from 8:54 to 17:20. Steroid medication use is also known to affect cortisol levels. Information on current prescription and non-prescription medications usage was collected and medications were dichotomised into steroid-related versus non-steroid-related medication or no medication. 40 (14%) participants had used steroid-related medications within the last 2 weeks; 27 reported cortisol-based cream use, 12 inhaled steroid use and 1 oral tablet steroid use. There were no significant differences in cortisol reactivity between children who had used steroid medication and those who had not ($p$ = .358 full sample, $p$ = .506 girls and $p$ = .738 boys). To account for any potential confounding effects on cortisol reactivity we ran a simple linear regression predicting cortisol reactivity from time of day and steroid medication use and used the residual score for the main analysis.

*CU traits.* CU traits were assessed by mother-report at 5 years using a combination of items from the APSD (41), the CBCL (40) and the Strengths and Difficulties Questionnaire (SDQ; 45). All items are rated on a three point scale. Items were selected based on inclusion in CU traits measures in other studies (46-49). We have previously created CU traits latent factor scores on this sample at ages 2.5, 3.5 and 5 years (50) by subjecting items to exploratory and confirmatory factor analyses in MPlus (51). The age 5 measure comprises 13 items which are listed in Table 5.7.1.1 (supplementary material) together with the factor loadings. The derived CU traits measure shows improved internal consistency (α = .83) compared to the APSD alone (α = .60) and partial strong factorial invariance by sex.

*Aggression.* Aggression was assessed by mother-report on a 5 item physical aggression questionnaire (52). The questionnaire consists of five items previously shown to yield aggression scores with stability from ages 17 to 29 months (50): kicks other children, bites other children, hits other children, gets in many fights and physically attacks others. Each item is rated on a three-point scale: 0 = *not true*, 1 = *somewhat or sometimes true*, 2 = *very true or often true*. The items were subjected to a confirmatory factor analysis in Mplus (48) and a factor score was extracted for analysis.

*Age 7 Procedures and Measures.* At age 7 intensive families completed a 3 hour lab assessment in the centre and extensive families completed a 2 hour home assessment, during which mothers completed the questionnaire measures. Mothers gave consent for their child's class teacher to complete a questionnaire about the child. Mothers and teachers were recompensed with shopping vouchers for their time.

*Aggression.* Mothers and teachers completed the same 5 item physical aggression questionnaire (52) as was used at age 5 years.

*Confounders.* To account for socio-demographic risk mothers' age at conception and deprivation were included as covariates in the main analysis. Deprivation was assessed using the Indices of Multiple Deprivation (IMD; 39) and a binary variable, with 1= most deprived quintile of UK neighbours versus 0 = all other quintiles, used for analysis. To account for the stratification, variables indicating whether the family was high or low risk allocation to the intensive sample were also included as covariates.

### *5.3.3 Analysis plan*

First, the age 7 years mother and teacher aggression items were modelled as a single latent variable using the gsem command in Stata version 14 (53). A factor score was extracted for all subsequent analysis. Bivariate associations were examined using Spearmans correlations and, where appropriate, polychoric correlations. The main analysis used multiple linear regression with robust standard errors, with predictors entered as a series of blocks using the nestreg command which provides a Wald test of whether the addition of each block produces a significant improvement in the model. The first block contained the confounding variables (including the two stratification factor variables) and the main effects of child sex, age 5 aggression and CU traits, to test as a first step whether CU traits showed incremental prediction to age 7 aggression over and above concurrent aggression at age 5. In the second block, cortisol reactivity was added to test for a main effect of cortisol reactivity on age 7 aggression. In the third, the interaction term between CU traits and cortisol was added to examine for moderation of the CU traits aggression association by cortisol reactivity. In the final block, interaction terms between CU traits and sex, and cortisol reactivity and sex, and the three way interaction between cortisol reactivity, sex, and CU traits, were entered, to test whether there was a sex difference in the moderation by cortisol reactivity. All variables were centred prior to creating interaction terms. Interactions were explored using the margins command to test the association between CU traits and aggression at mean and 1 SD above and below the mean levels of cortisol reactivity.

## 5.4 Results

### *5.4.1 Computation of physical aggression outcome*

The factor loadings for the mother and teacher aggression items on the single aggression latent variable are shown in Table 5.7.1.1 (supplementary material) for the extensive sample. A factor score was extracted for all subsequent analyses.

*5.4.2 Bivariate analysis*

The descriptive statistics for the key study variables are presented in Table 5.4.2.1 and the bivariate associations in Table 5.4.2.2**,** for boys and girls separately. There was no association between cortisol reactivity and concurrent CU traits or aggression or age 7 physical aggression. CU traits and both age 5 and age 7 aggression showed a moderate to large association in boys and a moderate association in girls. Mothers' younger age at pregnancy was significantly associated with higher aggression and CU traits in boys, with a marginal association between deprivation and CU traits, underlining the importance of controlling for these variables in subsequent analyses.

Table 5.4.2.1: Descriptive statistics for the key study variables for boys and girls separately

| | **Boys** | | **Girls** | |
|---|---|---|---|---|
| | **Mean (SD)** | **Range** | **Mean (SD)** | **Range** |
| *Age 7* | | | | |
| Physical aggression (teacher and mother report) | .68 (2.05) | -.79 – 7.22 | -.18 (1.33) | -.79 – 5.31 |
| *Age 5* | | | | |
| Baseline cortisol | 6.93 (4.33) | .81 – 27.28 | 7.64 (5.86) | 1.57 – 32.03 |
| Post-stressor cortisol | 5.85 (5.39) | .47 – 30.52 | 6.62 (5.77) | 1.49 – 30.52 |
| Cortisol reactivity | -1.09 (4.34) | -.15 – 20.30 | -1.01(3.78) | -9.14 – 16.68 |
| Aggression (mother report) | .45 (.69) | -.03 – 1.81 | .24 (.56) | -.03 – 1.81 |
| CU traits | .13 (.34) | -.51 – 1.20 | .02 (.34) | -.51 – 1.04 |
| *Confounding variables* | | | | |
| Mothers age at pregnancy | 27.30 (6.27) | 18 – 51 | 27.66 (5.94) | 18 – 41 |
| Most deprived: n (%) | 51 (35.2) | 0 – 1 | 56 (40.1) | 0 – 1 |
| Pregnancy stratification high risk: n (%) | 65 (44.8) | 0 – 1 | 61 (44.5) | 0 – 1 |
| Age 3.5 sample stratification high risk: n (%) | 38 (26.21) | 0 – 1 | 19 (13.77) | 0 – 1 |

Table 5.4.2.2: Bivariate associations between the key study variables by sex; boys on top diagonal and girls on bottom diagonal.

| | Age 7 agg | Age 5 agg | CU traits, age 5 | Cortisol react., age 5 | Mother age | Most deprived | Preg. strat. | 3.5 year strat. |
|---|---|---|---|---|---|---|---|---|
| Age 7 aggression | | .48*** | .40*** | -.04 | -.17* | .04 | .02 | .19* |
| Age 5 aggression | .30*** | | .39*** | -.01 | -.08 | .01 | .10† | .29*** |
| CU traits, age 5 | .32*** | .20*** | | .05 | -.19* | .14† | -.02 | .35*** |
| Cortisol reactivity, age 5 | .13 | .06 | -.03 | | .08 | .03 | -.09 | .05 |
| Mother younger age at conception | -.13 | -.11* | -.05 | .14 | | -.32*** | -.08* | -.19* |
| Most deprived | -.05 | .07 | .02 | -.13 | -.33*** | | .04 | .08 |
| Stratification in pregnancy | .07 | .14* | -.01 | -.06 | -.12** | .15* | | -.39*** |
| Stratification age 3.5 years | .03 | .14† | .11 | -.05 | -.04 | -.04 | -.31*** | |
| Mean (SD) | .26 (1.79) | .35 (.64) | .07 (.35) | -.02 (.95) | 27.47 (6.10) | .38 (.49) | .61 (.76) | .20 (.40) |

†$p < .10$, *$p < .05$, **$p < .01$, ***$p < .001$

### *5.4.3 Multivariate analysis*

The results of the main analysis using multiple linear regression are presented in Table 5.4.3.1. In the first block, after accounting for confounders, age 5 aggression significantly predicted later aggression, and age 5 CU traits were also a significant

predictor, consistent with previous findings that CU traits show incremental prediction of later problem behaviour after accounting for initial behaviour. In the second block, the main effect of cortisol reactivity was added, this was non-significant ($p$ = .816) and the block was not a significant improvement to the model ($p$ = 813). Block three, which introduced the interaction term between cortisol reactivity and CU traits, was a significant improvement ($p$ = .009), with the significant interaction term ($p$ = .010) providing support for the moderating role of cortisol reactivity in the prospective association between CU traits and aggression. The association between CU traits at age 5 and aggression at age 7 at low (1SD below mean), medium (mean) and high levels of reactivity (1SD above mean) is illustrated in Figure 1. CU traits significantly predicted aggression at low reactivity (dy/dx = 1.49, t = 3.54, p <.001) and at mean reactivity (dy/dx = 1.05, t=3.55 p < .001) but not at high reactivity (dy/dx = .62, t=1.38, p =.169).

In the final block, the three-way interaction between sex, cortisol reactivity and CU traits was significant ($p$ = .043) although the block itself fell short of conventional significant (p = .092). Two further linear regression models were then estimated to examine the two-way interactions between child CU traits and cortisol reactivity in boys and girls separately. The results are presented in Table 5.4.2.4. For boys, age 5 aggression was a substantial predictor of age 7 aggression, but CU traits also showed significant incremental prediction. For girls, only CU traits predicted age 7 aggression (p = .002). Significant main effects of cortisol reactivity were not found for either boys or girls, although the coefficients were in the opposite direction: negative in boys and positive in girls. The two-way interaction between CU traits and reactivity in girls was not significant (β = .03, $p$ = .751) and the coefficient slightly positive in direction, whereas the interaction in boys was significant and negative in direction (β= -.23, p < .001). The interaction in boys was explored using the margins command, CU traits significantly predicted aggression at low reactivity (dy/dx = 2.28, t = 4.40, p <.001) and at mean reactivity (dy/dx = 1.42, t=3.67, p < .001) but not at high reactivity (dy/dx = .56, t=1.38, p =.341). The association between CU traits and aggression at low, medium and high levels of reactivity in boys only is illustrated in Figure 5.4.3.2.

Table 5.4.3.1: Summary of linear regression model predicting age 7 aggression from age 5 cortisol reactivity, CU traits and child sex

| | **β** | ***p*** |
|---|---|---|
| *Block 1* | | |
| Mothers age | -.10 | .071 |
| Most deprived | -.05 | .306 |
| Sample stratification status: pregnancy stratum 1 | -.01 | .808 |
| Sample stratification status: pregnancy stratum 2 | .05 | .412 |
| Sample stratification status: 3.5 years | -.03 | .546 |
| Child sex | -.13 | .009 |
| Age 5 aggression | .32 | $p$<.001 |
| Age 5 CU traits | .19 | .001 |
| | $F(8, 275) = 22.77$, $p < .001$. $R^2 = .27$. | |
| *Block 2* | | |
| Cortisol reactivity | .01 | .816 |
| | $F(1, 282) = .06$, $p = .813$. $R^2 = .27$. $R^2\Delta = .00$ | |
| *Block 3* | | |
| CU traits * Cortisol reactivity | -.11 | .010 |
| | $F(1, 282) = .6.87$, $p = .009$. $R^2 = .28$. $R^2\Delta = .01$ | |
| *Block 4* | | |
| CU traits * Cortisol reactivity | -.29 | .004 |
| Child sex * Cortisol reactivity | .07 | .643 |
| Child sex * CU traits | -.24 | .163 |
| Child Sex * CU traits * Cortisol reactivity | .20 | .043 |
| | $F(3, 280) = 2.17$, $p = .092$. $R^2 = .29$. $R^2\Delta = .01$ | |

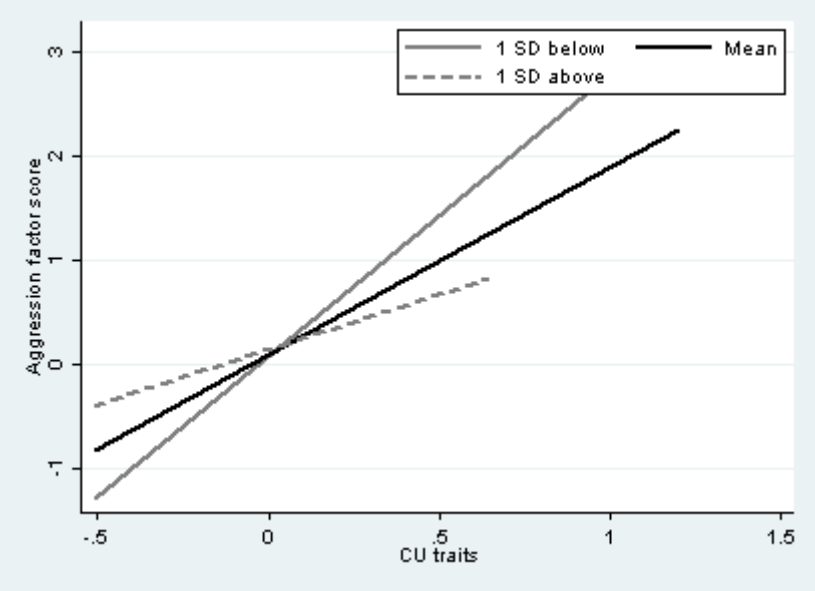


Figure 5.4.3.1: The prospective association between CU traits and aggression at 'low', 'medium' and 'high' cortisol reactivity

Table 5.4.3.2: Summary of linear regression model predicting age 7 aggression from age 5 cortisol reactivity and CU traits in boys and girls separately

| | **Boys** | | **Girls** | |
|---|---|---|---|---|
| | **β** | ***p*** | **β** | ***p*** |
| *Block 1* | | | | |
| Mothers age | -.09 | .254 | -.16 | .078 |
| Most deprived | -.03 | .700 | -.12 | .137 |
| Sample stratification status: pregnancy stratum 1 | .05 | .445 | -.06 | .416 |
| Sample stratification status: pregnancy stratum 2 | -.03 | .973 | .11 | .288 |
| Sample stratification status: 3.5 years | -.02 | .793 | -.02 | .766 |
| Age 5 aggression | .43 | .001 | .12 | .211 |
| CU traits | .22 | .008 | .28 | .002 |
| | $F(7, 138) = 3.86$, $p < .001$. $R^2 = .31$ | | $F(7, 131) = 2.00$, $p = .059$. $R^2 = .15$ | |
| *Block 2* | | | | |
| Cortisol reactivity | -.05 | .443 | .13 | .157 |
| | $F(1, 144) = 3.86$, $p = .324$. $R^2 = .31$. $R^2\Delta = .00$ | | $F(1, 137) = 2.03$, $p = .751$. $R^2 = .16$. $R^2\Delta = .01$ | |
| *Block 3* | | | | |
| CU traits * Cortisol reactivity | -.14 | .013 | .03 | .751 |
| | $F(1, 144) = 6.34$, $p = .013$, $R^2 = .32$. $R^2\Delta = .01$ | | $F(1, 137) = .10$, $p = .075$. $R^2 = .16$. $R^2\Delta = .00$ | |

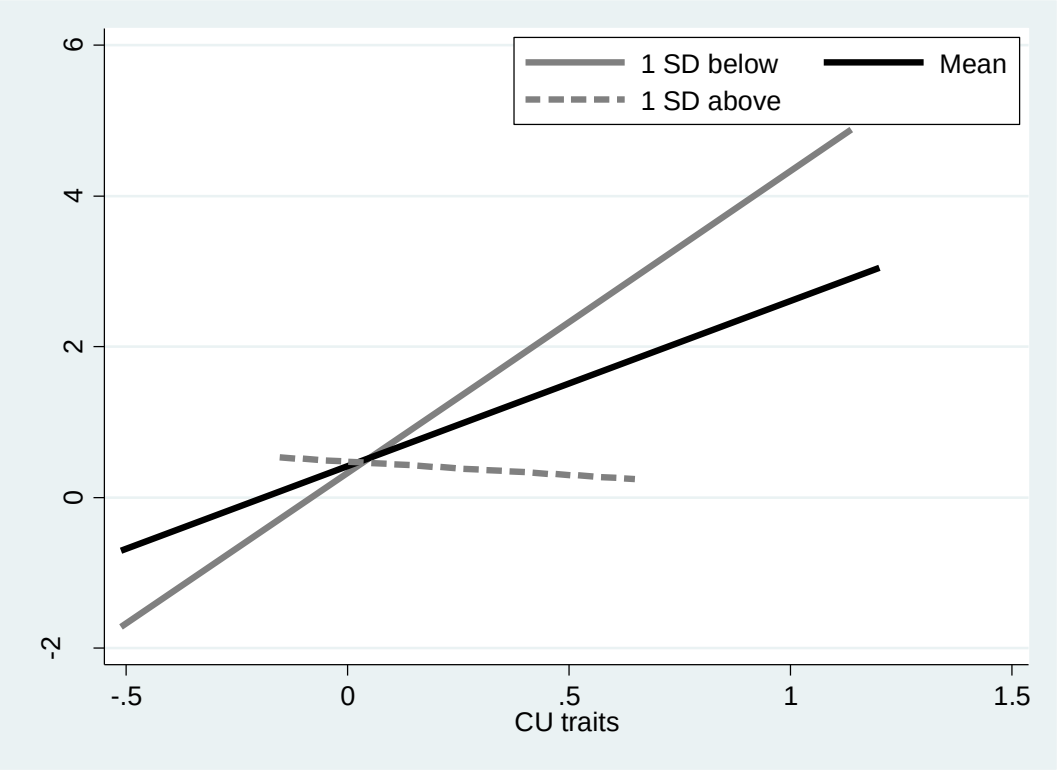


Figure 5.4.3.2: The prospective association between CU traits and aggression at 'low', 'medium' and 'high' cortisol reactivity in boys

## 5.5 Discussion

In a longitudinal general population sample with cortisol reactivity to a social stressor and CU traits assessed at age 5 years and physical aggression assessed at age 7 years, we showed that cortisol reactivity significantly moderated the association between CU traits and aggression. Further, a significant three-way interaction between cortisol reactivity, CU traits and child sex suggested that this was true for boys and not girls. In girls there was an association between CU traits and aggression that was similar at all levels of cortisol reactivity, while in boys the association was markedly different at low and high levels. CU traits at age 5 years strongly predicted age 7 aggression at cortisol reactivity levels 1 SD below the mean but not at 1 SD above. There were no main effects of cortisol reactivity on aggression, nor any

significant bivariate associations between cortisol reactivity and CU traits or aggression.

The findings are consistent with neurobiological models which implicate a role for reduced physiological arousal in the development of antisocial behavior (20, 21). However, they also support a growing literature implicating a low physiological reactivity pathway to externalizing problems in boys only. Previous findings have demonstrated associations between reduced RSA reactivity as an index of autonomic function (22-24) and reduced basal cortisol (27, 29) and externalising problems in boys. In this study, in light of only modest associations between CU traits and aggression, we sought to examine whether HPA-axis reactivity was a potential moderator in the association between CU traits and physical aggression. The results provided support for the moderating role of cortisol reactivity and this appeared to be the case in boys only. Prior studies have examined environmental and cognitive moderators (35, 36) and this is the first study to provide evidence for a biological moderator of HPA-axis reactivity. The findings suggest that in the context of reduced responsiveness to distress conferred by CU traits, reduced physiological arousal creates an elevated risk for aggressive behaviour. Theoretical accounts of the link between reduced HPA-axis activity and violent behaviour have proposed that low arousal creates a failure of inhibition (Fearlessness theory; 19) or acts as a driver for engaging in risky behaviour (Sensation Seeking theory; 20). A persuasive account of aggressive behaviour from Tremblay (54) draws on the well replicated finding that for most individuals' aggression decreases throughout childhood and into adulthood. Tremblay asserts that rather than children learning to become aggressive, they must learn not to use aggression. Within this framework both CU traits and reduced cortisol reactivity can be conceptualised as failures in inhibitory processes.

Age 5 CU traits significantly predicted age 7 aggression after accounting for concurrently assessed aggression, in both boys and girls, consistent with prior work showing that CU traits show incremental prediction of future problem behaviour over and above past problem behaviour (55). Interestingly, for girls, the association between age 5 and age 7 aggression was entirely explained by age 5 CU traits, consistent with a prior publication from this cohort over the age range 2.5 to 5 years (50). Very few studies examine for sex differences in associations between CU traits

and antisocial behaviour and this topic warrants further attention. We did not find any bivariate associations between cortisol reactivity and later physical aggression per se; with girls showing a small non-significant positive association between the two and near zero coefficients shown for boys. A recent meta-analysis of studies reported a great deal of inconsistency in findings across studies and so this lack of association is not unusual (25). Similarly we did not find associations between concurrently assessed CU traits and cortisol reactivity. One prior investigation has reported an association between higher CU traits and lower cortisol reactivity in a sample of boys with ADHD (33) but the authors did not investigate translation to aggression over time. The novelty of the current findings lie in the test of the moderating role of cortisol reactivity in the translation from CU traits to aggression over time.

The study was characterized by a number of strengths in the study design, sample and measurement. This was a prospective study of a consecutive sample from an antenatal clinic serving a defined geographical area. The sample was over-represented with children at risk for behavior problems, but inclusion of the sample stratification factors in the models allows generalisations to be made to the general population. Child CU traits and cortisol reactivity were assessed at age 5 and aggression was prospectively assessed two years later. Both teacher and mother report of aggression were collected at age 7. This allowed creation of an aggression outcome which sampled behaviour in multiple domains and also helped to reduce the effect of common method variance on the reporting of CU traits and aggression.

Limitations of the study include that the cortisol assessment was limited in the context of this ongoing longitudinal investigation. Three cortisol samples were deemed an acceptable demand on the sample, and priority was given to obtaining a more accurate baseline cortisol value and so only one post-stressor sample was taken. This limited the approach to analysis of cortisol reactivity. Cortisol assessments were also not completed at the same time of day for all participants, although we corrected for time of day in all analyses by creating a residualised cortisol score. We used an established social stressor paradigm to assess cortisol reactivity (43), however, the task does not include social-evaluative threat which has been identified as the most potent component of social stressor (56). Further some evidence suggests that males

and females respond differently to social versus achievement challenges (57) although to our knowledge this has not been demonstrated in children. We chose physical aggression as our outcome variable as violence is a key feature of the antisocial behaviour shown by children and adults with CU traits. However, other forms of aggressive behaviours, such as relational aggression, have also been linked to CU traits (58) and may be relevant. Finally, the sample is almost exclusively White British so the findings may not be not generalizable to other ethnic groups.

This study addressed the often neglected yet important question of how CU traits translate into aggressive behavior. From an epidemiological longitudinal sample followed up over two years, the findings provided first evidence for a biological moderator in the form of HPA-axis reactivity. Further, this was clearly a male specific mechanism, consistent with a growing literature on sex differences in risk from physiological arousal. Future research should seek to replicate this finding in older samples, given the evidence for changes in cortisol responsivity in adolescence (59). Further investigation of the potential processes involved in the translation of CU traits into aggressive behaviours, and whether these are sex-specific, is an important avenue for future research.

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## 5.6 Supplementary Material

Table 5.6.1.1 *Standardised factor loadings for the age 5 years CU traits measure*

| Age 5 CU traits items | Factor loading |
|---|---|
| APSD 1: Concerned about the feelings of others (R) | .47 |
| APSD 3: Is good at keeping promises (R) | .47 |
| APSD 4: Feels bad or guilty when he/she does something wrong (R) | .62 |
| APSD 5: Keeps the same friends (R) | .61 |
| CBCL 14. Cruel to animals | .60 |
| CBCL 58: Punishment doesn't change his/her behavior | .72 |
| CBCL 67: Seems unresponsive to affection | .77 |
| CBCL 70: Shows little affection toward people | .84 |
| SDQ 1: Considerate of other people's feelings (R) | .75 |
| SDQ 4: Shares readily with other children (R) | .53 |
| SDQ 9: Helpful if someone is hurt, upset or feelings ill (R) | .57 |
| SDQ 17: Kind to younger children (R) | .60 |
| SDQ 20: Often volunteers to help others (R) | .46 |

*Note*. CBCL = Child Behavior Checklist (CBCL), APSD = Anti-Social Process Screening Device, BITSEA = Brief Infant Toddler Social and Emotional Assessment (BITSEA), SDQ = Strengths and Difficulties Questionnaire (SDQ) .

Table 5.6.1.2: *Unstandardised factor loadings for the teacher and mother reported aggression items*

| | Unstandardised factor loading mother report | Unstandardised factor loading teacher report |
|---|---|---|
| Bites other children | 1.11*** | 1.21** |
| Kicks other children | .90*** | 2.40* |
| Hits other children | .66*** | 1.54*** |
| Gets in many fights | .65** | 1.00*** |
| Physically attacks others | .55*** | 1.90** |

# Chapter 6: Discussion

The primary goal of this thesis was to provide a further understanding of CU traits measured in the early childhood period covering from toddler to school entry age. More specifically, in the first empirical paper (Chapter 3) the psychometric properties and reliability of a hybrid measure of CU traits were examined at age 2.5 and 5 years and validity was assessed by examining associations with physical aggression. In the second paper (Chapter 4), the contribution of parenting in infancy to early childhood CU traits was examined, and specifically the prediction from different components of parenting (warmth/positive regard, sensitivity to distress, sensitivity to non-distress and intrusiveness) was tested, and whether any associations found were mediated or moderated by attachment security. Finally, the third paper (Chapter 5) investigated a possible mechanism through which CU traits may translate to aggressive behaviour. The moderating role of cortisol reactivity in the association between CU traits and aggression from age 5 to 7 years was examined, and based on a literature demonstrating sex differences in risk from physiological reactivity, a reduced reactivity pathway in boys was predicted.

## 6.2 Summary, interpretation, and integration of findings with directions for future research

### *6.2.1 Early measurement of CU traits*

The first study (Chapter 3) sought to address a number of issues regarding the measurement of CU traits, some of which have been present in measurement of CU traits throughout childhood and adolescence, and others specific to measurement in the early childhood period. These included that measures often show poor internal consistency, are rarely examined for invariance by sex, that the developmental appropriateness of CU items in standard measures have rarely been considered when used with younger children, and that developmentally appropriate hybrid measures typically have not included items assessing lack of concern for others. In this study, exploratory and confirmatory factor analysis was used on a larger pool of items from an existing CU traits measure and other early childhood problem behaviour

measures. The primary interest was to examine the psychometric properties of the measure at age 2.5 years, as very little research had examined CU traits at this age, and a previous study (Hyde et al., 2013) found poor psychometric properties for a measure at age 2 years. Age 5 is currently considered a more established age point for the measurement of CU traits, however, in this study a similar approach was taken to create an age 5 years measure as problems with poor internal consistency have been found for measures throughout childhood and adolescence, and the main measures for CU traits were developed with school age and adolescent children as the target samples.

The study was successful in producing CU traits scales which showed adequate psychometric properties evidenced by acceptable model fit and internal consistency at age 2.5 years and at 5 years. Mothers' CU traits ratings were distinguishable from physical aggression ratings. In Chapter 4, the same approach was taken to create and evaluate an age 3.5 years CU traits scale and this measure also showed acceptable psychometric properties. The items used at each age were allowed to vary to allow for developmental differences in the manifestation of CU traits at each age. Strong factorial invariance by sex was demonstrated for the age 2.5 and 3.5 years measures, with partial factorial invariance achieved for the age 5 measure.

The items in the CU traits measure created in this study include the key APSD items which assess lack of concern for others (or "callousness" as labelled in the ICU) and lack of guilt or remorse (labelled as "uncaring" in the ICU). Absence of prosocial behaviour and cruelty to animals also index a lack of concern for others/callousness. The APSD item designed to assess unemotionality ("does not show emotions") was dropped at the EFA stage due to problems with empty cells in in the cross-tabulation with other items. This item has consistently shown poor item-total correlations (Poythress et al., 2006) or failed to load with the other items in factor analysis (Dadds et al., 2005) which was also the case at age 5 in this sample. Similarly, the unemotional subscale of the ICU, which is an expanded version of this APSD item, has shown weak associations with the other two subscales and with external correlates (Kimonis et al., 2008; Waller et al., 2015). Shallow and deficient emotional expression is a key component of psychopathy; however, the wording of

the items designed to assess unemotionality on the ICU and APSD seems to assess *hiding* of emotion rather than absence or shallowness (Hawes et al., 2014). In the present study, at age 2.5 years, the decision was made to retain the two items from the CBCL which indexed lack of affection shown and unresponsiveness to affection in favour of the APSD "does not show emotions" item. These two items are included in the five-item CBCL based measure of CU traits used in early childhood (Willoughby et al., 2012) but also likely do not assess the construct of unemotionality as it is intended and are narrowly focused on affection. Another CBCL item which assessed absence of fear of getting hurt was not retained at age 2.5 and 5 years due to low factor loadings, but this item also has a rather narrow focus. Therefore the measure created in the present study does not adequately assess the construct of unemotionality, but arguably the other current gold standard measure of CU traits, the ICU, does not either. Overall much more work is needed examining the 'unemotional' component of psychopathy and CU traits. For example, it has rarely been considered whether these constructs are characterised by reduced emotionality across all the emotion domains or if individuals with CU traits, for example, show normative levels of happiness but reduced sadness and fear (Lahey, 2014).

The CU traits scales showed moderate to high stability over time; latent factor correlations between age 2.5 and 5 years scales were presented in Chapter 3 and spearmans correlations between both the factor scores and the mean item scores for the age 2.5, 3.5 and 5 measures were presented in Chapter 4 supplementary material. To facilitate comparison to previous investigations of stability in older child samples, and as an addendum to the analyses presented in the empirical chapters, ICC's were calculated following the same procedures as Frick, Kimonis, Dandreaux, and Farrell (2003) (see Appendix 3). An overall stability from the three measures spanning from age 2.5 to 5 years of ICC = .78 was achieved in the present dataset, which is smaller than estimates reported from samples of older children, but not substantially smaller. Frick et al. (2003) reported an ICC of .90 (n = 94) from four time points from age 8 to 12 years and Barry, Barry, Demin, and Lochman (2008) reported an ICC of .83 (n = 80) from three time points over three years from age 9 to 12 (ICC = .83, n =80). Thus the present thesis provided support for moderate stability of CU traits over the early childhood period.

Physical aggression was chosen as the key criterion variable to assess the validity of the age 2.5 CU traits measure. As reviewed in Section 1.8 and Chapter 3 and Chapter 5, the most important function of the psychopathy and CU traits constructs is their utility in identifying a subgroup of antisocial individuals who show more severe aggressive behaviour. In adults and adolescents, outcomes such as violent offending can be examined whereas in childhood samples it is necessary to focus upon the behaviours. The vast majority of measures in childhood do not assess physical aggression alone, with scales typically mixing physically aggressive items and non-violent forms of aggression (e.g., threatening others) together with broader oppositional and defiant behaviours (Tremblay, 2000). Throughout this thesis a measure of pure physical aggression was used which focused on mainly aggressive behaviours displayed towards peers. The age 2.5 years CU traits measure showed a significant cross-sectional association with physical aggression for both boys and girls, and the same result was found for age 5 years, providing support for the validity of the measure and for the construct of CU traits at these ages. The key test of validity, however, was whether CU traits showed incremental prediction in predicting physical aggression at age 5 after accounting for age 2.5 year aggression, age 2.5 and age 5 years CU traits, and all possible cross-sectional and longitudinal associations between them. Significant incremental prediction was found for girls but not for boys. However, this result must be considered in the context of the very strong continuity in aggression found for boys and not girls (standardised estimates of .84 and .02, respectively, in the sem model). In Chapter 5, the incremental prediction from age 5 CU traits to age 7 aggression, after accounting for age 5 aggression, was examined in linear regression. Incremental prediction was found for both boys and girls, although interestingly again for girls once CU traits were included in the model age 5 aggression did not significantly predict later aggression. However, it is important to bear in mind that the analysis in Chapter 5 provided a much less stringent test than the analysis in Chapter 3 where all possible cross-sectional and prospective associations between the variables were included in the modelling.

A number of potential interpretations of the lack of incremental prediction in boys at age 2.5 years were offered in the Chapter 3 discussion which suggest multiple directions for future research. This includes the possibility that the continuity in

aggression over that age period in boys is so strong that there was little remaining variance for CU traits at age 2.5 years to explain. It may be that the key risk processes occur prior to age 2.5 years in boys. In order to test this possibility, future studies would need to attempt to measure CU traits, or their precursors, prior to 2.5 years. Previous studies have identified infancy precursors to CU traits, including reduced face preference (Bedford, Pickles, Sharp, Wright, & Hill, 2013) and reduced-mother directed gaze in interaction with reduced negative reactivity in the still-face (Wagner et al., 2016). Examining the role of these precursors in the onset of aggression in boys could provide a test of this potential explanation of the findings.

Another potential interpretation is that, in boys, the translation of CU traits into aggression is dependent on other influences, for example, deficits in behavioural inhibitory processes, so that even in the absence of a main effect, effects may have been found in interaction with other variables. This possibility was examined over a different age range in Chapter 5. From age 5 to 7 years, CU traits showed a main effect predicting increased physical aggression in boys but also showed a significant interaction with reduced cortisol reactivity, such that the combination of higher CU traits and lower cortisol reactivity predicted increased aggression. This analysis was conducted using linear regression so did not test for moderation in the context of the other associations between CU traits and aggression, although age 5 aggression was accounted for in the model. It was also conducted over a later age range and a main effect of CU traits to aggression was achieved in that analysis for boys. However, it does provide support for the general hypothesis that the risk for aggression may be increased in the presence of other failures in behavioural inhibitory processes, such as reduced cortisol reactivity.

Finally, it may be that the CU traits construct is not valid in young boys because the relevant empathic processes develop later in boys than girls (Rhee et al., 2013), or the measure created may not be valid because the behaviours that reflect CU traits are not identified in the items of our existing measures. The CU traits measure showed equally strong stability from age 2.5 to 5 years for both boys and girls, with boys evidencing a slightly larger factor correlation (.75 compared to .71) which one might argue suggests that the age 2.5 CU traits measure is assessing a similar construct to the age 5 measure. This same age 5 CU traits measure showed

significant prediction to age 7 mother and teacher reported aggression in boys, after accounting for age 5 aggression and family demographic risk in Chapter 5. Future research should further examine the manifestation of CU traits in boys and girls separately, particularly at this younger age. Examination of associations with other relevant correlates to CU traits, such as early empathy and fearlessness, in boys and girls separately, may be one way to address this question. In this study the CU traits items were selected using EFA and CFA on the sample as a whole and then measurement invariance by sex was examined for those items. Of the three ages, the age 2.5 and age 3.5 measures achieved full scaler invariance whereas the older age point, 5 years, only achieved partial invariance. However, future studies with a larger sample at age 2.5 years, may want to test out selecting appropriate CU items separately in boys and girls.

### *6.2.2 Parenting environment and CU traits*

The second aim of this paper was, broadly, to examine the contribution of parenting at age 7 months to later childhood CU traits, and more specifically, to test and compare the contributions of some specific components of 'positive parenting'. We also examined whether any associations found were mediated or moderated by mother-infant attachment status assessed at 14 months of age. As CU traits are characterised by reduced responsiveness to distress in others, we hypothesised that the experience of having one's own emotions responded to empathically would promote that ability in oneself. A latent variable approach was taken to model the prediction of child CU traits assessed at age 2.5, 3.5 and 5 years, from four key parenting variables from the NICHD coding scheme. The four chosen variables included sensitivity to distress, sensitivity to non-distress, warmth and intrusiveness. Prediction from the overall parenting factor comprised of all four variables was tested, along with prediction from each variable, and finally whether adding a direct path from each variable to child CU traits showed specific prediction over and above that from the general factor. As expected, the general parenting factor formed from increased sensitivity to distress, increased sensitivity to non-distress, increased positive regard and decreased intrusiveness predicted reduced child CU traits. Further, consistent with predictions, sensitivity to distress and not non-distress

significantly predicted reduced child CU traits when considered individually. When a direct path from sensitivity to distress was added from the factor to child CU traits, the prediction from the factor became non-significant, but the path from sensitivity to distress itself did not reach conventional levels of significance. Positive regard also showed a similar prediction to child CU traits as sensitivity to distress in the individual models, then when a direct path was added from the general parenting factor this also rendered the prediction from the general factor non-significant and the path from positive regard was significant. In contrast to a priori prediction, positive regard appeared the stronger predictor of the two. The two variables did evidence a synergistic effect, evidenced by a significant interaction whereby the combination of high positive regard and high sensitivity to distress predicted reduced CU traits.

Thus the study did not provide evidence that maternal sensitivity to distress was a better predictor of child CU traits than maternal warmth. This had been shown previous in a sample of two to three year old boys predicting CU traits in adolescence (Humphreys et al., 2015) and a sample of 6-8 year old children predicting concurrently assessed empathy (Davidov & Grusec, 2000). It may be that parental sensitivity to distress becomes more closely linked to CU traits once the child has begun to develop empathy related processes in the second and third years of life (Kochanska, Gross, Lin & Nicholas, 2002; Vaish, Carpenter & Tomasello, 2009). Differences in the coding may also explain the pattern of findings. Sensitivity to distress was coded in the current study from any distress cues shown in a 15 minute semi-structured free-play task and so the coding could be based on a very small number of instances, whereas positive regard could be coded from the entire interaction. In Humphrey et al. (2015) the coding of warmth and sensitivity to distress were made over a longer period of time in the home, which allows for more potential instances of distress, although this will still suffer from disproportionate opportunities to code warmth and sensitivity to distress. In future studies, when comparing parenting coded from the same task, attempts at weighting the coding to reflect the proportion of the interaction that distress was shown should be made. Other studies have coded sensitivity to distress from tasks designed to be distressing such as the Still-Face Procedure (e.g. Leerkes, 2011) which allows the coding to sample more instances of response to distress. These approaches are both viable

options to assess sensitivity to distress with infants who show distress more frequently. However, when investigating sensitivity to distress in older children there would likely not be enough instances of distress to code from free-play or natural observation unless very long period of time are sampled, and it may not be ethically feasible to use tasks designed to cause distress. With 6-8 year olds, Davidov and Grusec (2000) took a multi-method approach and used a combination of self-report questionnaires and parental responses to viewing a video of a distressed child. This approach combats the need to cause distress to the child in the lab, but self-report measures are likely to be subject to social desirability biases. Future research needs to consider these methodological concerns carefully, especially if attempting to extend the current findings to older children.

Overall, the present findings make an important and novel contribution to the literature by providing evidence for the role of maternal sensitivity to distress in infancy in later reduced child CU traits. In this study sensitivity was measured at 7 months, however, as highlighted in the Chapter 4 discussion, maternal sensitivity measured even earlier has been linked to poorer child outcomes in other studies (e.g., 2 months; Hentges et al., 2011) which makes the case for examination of parent-infant interaction and later outcomes with measurements at multiple points over the first year of life. This approach could identify key periods for the influence of sensitivity to distress in development which would have important implications for intervention. It would also be interesting to examine how mothers' characteristics contribute to her ability to respond to distress, particularly within the context that mothers themselves may have CU traits. This last point highlights another important issue in research on maternal positive parenting practices and child CU traits, the possibility of gene-environment correlations. Future research should attempt to account for this, for example, by using adoption designs (e.g. Waller et al., 2017). Another exciting avenue for future research will be to explore the interplay between maternal parenting characteristics and low infant eye gaze across early development. Finally, as reviewed in the introduction, some studies have found evidence for sex differences in the association between parenting and child CU traits. We were not able to examine for sex differences in the current analysis due to concerns about statistical power. This will be an important topic for future research.

In this study we found no association between attachment security or disorganisation and child CU traits, therefore there was no evidence for mediation of the association between maternal parenting and child CU traits by attachment status. There was also no evidence for moderation by attachment status. A previous study with an older clinical sample had found associations between CU traits and attachment insecurity and disorganisation, assessed using a story completion attachment task (Pasalich, Dadds, Hawes, & Brenna, 2012). In another study, attachment disorganisation assessed at 3 years using a modified strange situation procedure was associated with a stronger association between the combination of ODD and CU traits and aggression, although attachment showed no bivariate association with CU traits (Willoughby, Mills-Koonce, Gottfredson, & Wagner, 2014). The present sample was well suited to test the prediction from attachment disorganisation as a large proportion of the sample were identified as disorganised, but we found no evidence for an association. It may be that attachment processes contribute to risk of CU traits only after infancy, further studies examining links from infant attachment status to later CU traits are needed. Alternatively, it may be that attachment contributes to CU traits specifically in the context of conduct problems, which would be consistent with the findings from Willoughby et al. and Pasalich et al. Future research with sufficient numbers of children with CU traits with and without conduct problems should test this possibility.

Theoretically, we would argue that disorganised attachment status does not seem to be the most relevant attachment classification for the development of CU traits. The defining feature of disorganised attachment status is the lack of coherent emotion regulatory strategies in the context of separation from the mother. Incoherence has not been proposed to be a feature of CU traits, rather, CU traits have been conceptualised as a consistent unresponsiveness to threat and distress. Similarly, those behaviours associated with a resistant attachment status, characterised by high emotional dysregulation, do not seem to reflect conceptualisations of CU traits either, although one study has reported that higher negative emotionality in infancy predicts later CU traits accompanied by ODD (Mills-Koonce et al., 2015). In contrast, the behaviours displayed by an infant classified as insecure avoidant (showing little distress, not seeking comfort from the mother, avoiding her on reunion) actually appear more characteristic of a child with

CU traits. An interesting avenue for future research would be to explore the association between the individual attachment classifications and later child CU traits, if possible in samples at higher risk for CU traits to ensure sufficient numbers. Rates of disorganised attachment are much higher in samples who have experienced maltreatment or violence (Carlson, Cicchetti, Barnett, & Braunwald, 1989; Zeanah et al., 1999) and so disorganised attachment may be more relevant to the development of secondary psychopathy which is hypothesised to arise from traumatic experiences (Porter, 1996) which may explain the absence of a main effect found in this study, and could be examined in future research.

The finding that sensitivity to distress and warmth, but not attachment status, predict reduced child CU traits, suggests that the beneficial impact of these practices in infancy does not operate through emotional regulation with a caregiver. Rather, there may be another route whereby parental warmth and sensitivity promote emotional and social understanding and responsiveness more generally. Sensitivity to distress may specifically promote empathic responding via processes such as modelling (Kiang, Moreno, & Robinson, 2004) or imitation (Baird, Scheffer, & Wilson, 2011). Whether this transmission needs to occur from attachment figures or if promotion of empathic responding can be learned from experience or observation of sensitive responding to distress and warmth from peers, siblings or other adults such as childcare providers would be an interesting topic for future research and have implications for intervention.

Finally, the only index of 'negative' parenting practices assessed in the investigation, namely intrusiveness, was not associated with CU traits. To our knowledge this is the first study to examine the association between intrusiveness and child CU traits. Maternal intrusiveness has been linked to child behavioural problems (e.g. Egeland, Pianta, & O'Brien, 1983) although an intrusive and over-controlled parenting style has been more consistently linked to child anxiety (Van Der Bruggan, Stams & Bogels, 2008) and theoretically appears more closely linked to internalising problems then externalising problems.

### *6.2.3 The role of cortisol reactivity in the translation of CU traits to aggression*

CU traits were downwardly extended to childhood to subtype conduct problems and they have proved effective in this endeavour. However, associations between CU traits and conduct problems, and CU traits and aggression, the focus of this thesis, are moderate in size. Surprisingly, the question of why some children with CU traits go on to develop aggressive behaviour and others do not has rarely been examined in the literature. In this thesis, we examined one candidate biological moderator of the association between CU traits and aggression, namely reduced HPA-axis reactivity. Reduced physiological arousal had previously been implicated in the development of antisocial behaviour, but findings from studies examining both broad externalising problems (Alink et al., 2008) and CU traits (e.g. Loney, Butler, Lima, Counts, & Eckel, 2006; Poutska et al., 2010) had returned rather inconsistent findings. Two potential factors were considered to help account for the inconsistency. Firstly, for studies of broad externalising behaviour, there is reason to suppose that reduced physiological arousal would be relevant to the subtype of externalising problems characterised by CU traits, and not for so called 'hot' conduct problems characterised by anger and emotional over-reactivity (Hawes, Price, & Dadds, 2014). Secondly, findings from both animal and human work suggest that there are important sex differences in the risk for and in the risk from physiological arousal, with *low* arousal creating the risk for males and *high* arousal the risk for females (e.g. Costello, Worthman, Erkanli, & Angold, 2007; Frye & Wawrzycki, 2003; Zagron & Weinstock, 2006; Tibu et al,., 2014; Dietrich et al., 2013). Thus the evidence suggests that reduced cortisol reactivity would seem to be relevant for the narrower externalising problem phenotype characterised by CU traits, and for males only. We hypothesised that reduced cortisol reactivity would moderate the association between CU traits and later aggression in boys only.

The results were consistent with the hypothesis. There was a significant two-way interaction between CU traits and cortisol reactivity, such that CU traits were significantly positively associated with physical aggression at low and mean levels of cortisol reactivity but not at high levels of cortisol reactivity. The addition of a three-way interaction between sex, CU traits traits and cortisol reactivity, was also

significant, although the block did not represent a significant improvement to the mode. When the two-way interaction was examined in boys and girls separately, the moderation by low cortisol reactivity was clearly present for boys. For girls, cortisol did not moderate the association between CU traits and aggression. The findings were interpreted within Tremblay's (Tremblay & Nagin, 2004) theoretical account of the development of aggressive behaviour, which, based on the evidence that aggression declines throughout childhood into adulthood, proposes that during childhood most individuals learn to regulate their inherent aggressive behaviour. Within this framework, both CU traits and reduced cortisol reactivity can be conceptualised as failures in inhibition. CU traits create failure from the lack of responsiveness to others distress, which would typically inhibit the infliction of suffering on others, and reduced cortisol reactivity, which according to fearlessness theory (Raine, 1996) creates failure by reducing the ability to learn from sanctions about misbehaviour. In this sample, low cortisol reactivity was associated with the lowest aggression in the absence of CU traits, indicating that low reactivity in the absence of CU traits was actually protective for the development of aggression. This makes intuitive sense; low cortisol reactivity creates a failure of inhibition, and in the context of an indifference to others distress this leads to aggressive behaviour.

Rather than focusing on low physiological reactivity as a risk for aggressive behaviour, Raine has conceptualised increased physiological reactivity as a protective factor. In two different samples, Raine has demonstrated that increased physiological reactivity assessed via skin conductance was protective for males at risk for criminal behaviour by virtue of having a criminal father (Raine, Reynolds, Venables, Mednick, & Farrington, 1995; Brennan et al., 1997). In the present study, the two-way interaction in boys was explored by creating groups at the mean level of reactivity and one standard deviation above and below the mean. As can be observed on the plot (Figure 5.4.3.2, page 142), the group identified as 'high' reactive had a narrower range and lower CU scores than those at the mean and at low cortisol reactivity levels, thus we did not find that any high reactive boys had very high CU traits scores. The present findings might therefore conceivably be viewed as supporting the idea that higher reactivity is somewhat protective for boys. However, we also observed the lowest level of aggression in boys with low CU traits and low

cortisol reactivity, so in fact in this sample low CU traits and low reactivity were the most protective combination for boys.

Reduced physiological arousal has played a key role in conceptualisations of CU traits and of conduct problems accompanied by CU traits, as well as in adult psychopathy. The present findings from this prospective study implicate reduced reactivity in the translation of CU traits to aggressive behaviour in boys, rather than being characteristic of CU traits per se since we found no bivariate association between cortisol reactivity and CU traits. These findings might be viewed as consistent with reports of associations between reduced physiological reactivity and CU traits in samples with behavioural problems, or with findings from criminal samples with psychopathy, since these samples are likely to comprise of aggressive individuals. The only other study with a youth sample, Stadler et al. (2011), reported an association between CU traits and reduced cortisol reactivity, with their 'high' CU group showing significantly lower cortisol reactivity than their 'low CU' group. They did attempt to show that this finding was independent of behavioural problems in the sample by controlling for these in analyses. However, the authors used the CBCL total problems score to do this which reflects more internalising than externalising difficulties. Further, the significant difference in cortisol reactivity between the groups with and without CU traits was found at 35 minutes post stressor, and not 20 minutes post-stressor, which was used in the current study.

It is also relevant that this previous study used an adolescent sample whereas the current study used a young school-aged sample. A meta-analysis of all studies examining cortisol responses and child externalising problems did report evidence for age differences in their results, with associations found at preschool and school age but not in adolescence (Alink et al., 2008). Adolescence appears to be a time of change in HPA-axis reactivity; adult males consistently show a higher HPA-axis response relative to females, but this difference is not found in childhood and appears to emerge during mid to late-adolescence. Whether this change is related to pubertal development or other factors is yet unknown (Ordaz & Luna, 2012). Therefore it seems important that the present findings are replicated in samples of different ages.

The present findings are consistent with the literature reviewed in chapter 5 regarding sex differences in risk from physiological arousal in so much as we found that reduced reactivity is a male specific pathway. Although studies of basal cortisol or diurnal cortisol rhythm reflect different processes than cortisol reactivity, and the present analysis examined the role of cortisol reactivity in the translation to aggression not in relation to CU traits per se, it is worth noting that in the one study to assess basal cortisol and CU traits in a mixed sex sample, an inverse association between CU traits and cortisol was found in males and no association in females (Loney et al., 2006). A rather consistent finding emerging in the literature is that females with CU traits are more likely to have accompanying anxiety or internalising problems than males ( Essau, Sasagawa, & Frick, 2006;Euler et al., 2015; Meehan, Maughan, Cecil, & Barker, 2017). This has not yet been demonstrated in a sample of school-age children such as that used in the present study. However, this does suggest that CU traits in females may be characterised by more negative affect and higher physiological arousal than for males, which could be consistent with the translation of CU traits to aggression not following a reduced physiological reactivity pathway.

As low cortisol reactivity is considered a physiological marker for low fear or low behavioural inhibition (Raine, 2002; Nigg, 2006) the present findings may suggest that the hypothesised 'fearlessness' pathway to CU traits could in fact be the pathway from CU traits to aggressive or antisocial behaviour. Further, the findings suggest that this may be specific to males only. Surprisingly few studies have examined links between CU traits and fearlessness and none have examined for sex differences are far as we are aware. Future studies should examine the role of fearlessness in the development of CU traits and in the translation of CU traits to aggression in mixed samples of males and females and test for sex differences. However, as highlighted in section 6.2.1, the measure used in the present study, and other gold standard CU traits measures, likely do not adequately assess the unemotional component of CU traits/psychopathy. Therefore it is also important to replicate the present findings, and to assess associations with other markers of low fear, with a measure that adequately assesses the unemotionality dimension of CU traits. Another important avenue for future research is to examine for other potential moderators of the association between CU traits and aggression. The identification of

moderators may permit us to predict which children with CU traits will go on to develop aggressive behaviour. In particular, in future research careful consideration should be given to identifying potential moderators for females, which could be informed by a greater research focus in general on CU traits in female samples.

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## 6.3 Limitations

Each empirical paper contains its own summary of the limitations relevant to that specific study; this section will include a discussion of some overarching limitations with the thesis research. The first pertains to the sample. The sample is characterized by a great number of strengths including that it is representative of the socio-ecomonic spread of the area it was drawn from and comprises a large proportion of deprived families, that the sampling design allows more detailed study of a subsample with heightened risk but also retains a larger general population sample, and that the sample has had repeated follow up throughout pregnancy and childhood. However, the sample is almost exclusively White British and so the results cannot be generalized to other ethnic groups. Further, although the sample is relatively high risk in terms of deprivation, and the intensive subsample was stratified on the basis of reports of psychological abuse within the parental relationship, overall it is still a community sample and rates of aggressive behavior and of CU traits reflect that. The relatively low levels of endorsement of CU traits and aggression on some items of the measures used necessitated some collapsing of item response categories for the analysis in Chapter 3.

Another overarching limitation relies in the use of maternal report for many of the measures, which meant that some analyses were subject to the effects of shared method variance, particularly the analysis in Chapter 3. We were not able to collect teacher report until age 7 when all the children were all in full-time school. Father report was collected at some of the earlier ages but fathers were not available for all children in the sample. Where possible sociodemographic risk factors and maternal mood at time of reporting were included in the statistical analysis of the data to try and remove some of the potential bias in ratings, but over-reliance on mother report

remains a limitation. Further, given the focus on sex differences in associations with aggression in this thesis, an observed measure of aggression would have been beneficial due to evidence of sex-based bias in the reporting of aggression for girls. Studies have shown that raters are less likely to interpret female behavior as aggression (Condry & Ross, 1985; Lyons & Serbin, 1986; Susser & Keating, 1990) although in this study the use of a pure physical aggression items in the outcome measure should hopefully have reduced some of this bias since overt physical aggression is more difficult to misinterpret than more indirect forms of aggression. A final overarching limitation is that the CU traits measure created in the present study likely does not adequately assess the unemotional component of CU traits. This may have affected the results presented in the three papers in this thesis.

## 6.4 Implications for practice

The findings from this thesis have important implications for clinical practice. In Chapter 4, sensitivity to distress in infancy was found to predict reduced childhood CU traits, implicating a potential new target for intervention. Positive regard (warmth) and sensitivity to distress showed a significant interaction, such that the combination of both predicted reduced CU traits scores compared to either alone. There has been controversy in the literature as to whether children with CU traits are able to benefit from intervention, with some studies demonstrating that CU traits moderate the effect of intervention on conduct problems, such that children with CU traits showing less improvement than children without CU traits (e.g. Hawes & Dadds, 2005; Kolko & Pardini, 2010; Masi et al., 2013; Waschbusch, Carrey, Willoughby, King, & Andrade, 2007). However, as reviewed by Waller et al. (2013) several parenting-focused prevention and targeted interventions have been shown to lead to reductions in child CU traits. In particular, interventions which include a focus on increasing parental warmth have led to reductions in the level of CU traits in young children (Dadds et al., 2012, 2013; Kimonis, Bagner, Linares, Blake, & Rodriguez, 2014). Both warmth (Pasalich et al., 2016) and responsiveness to distress (Humphreys et al., 2015) have been found to mediate the effects of a parent-based intervention on CU traits with samples aged 2-5 years. The present findings suggest that targeting both warmth and responsiveness to distress may be particularly

beneficial, and responsiveness to distress has appeal as an intervention target. Currently, Dadds and colleagues are running a trial evaluating an intervention that seeks to increase eye contact from children with CU traits to attachment figures and involves directing parents to maintain eye contact with the child and express love towards them on regular occasions (http://www.isrctn.com/ISRCTN62822052). One can imagine that this therapeutic approach may be difficult for parents who may themselves have CU traits and are likely experiencing difficulties in the parent-child relationship. Increasing responsiveness to distress is appealing as an intervention target as it is a tangible practical skill that may be easier for parents of children with behavioural problems to adopt.

The present findings also have implications for early intervention. This study is one of the first to identify infancy predictors of later child CU traits. With further replication, the findings suggest that intervention in infancy in families at high risk for CU traits may be possible. With promising research on very early infant antecedents of child CU traits, such as low eye gaze, there is potential that interventions can be implemented and their effects evaluated in infancy. Also, the finding that CU traits can be reliably measured at age 2.5 years provides an early age point for reliably measuring CU traits themselves as a treatment outcome. Further, our finding that age 2.5 CU traits predicted aggression at school entry age (at least in girls) suggests a role for intervention with CU traits in the preschool period. Tremblay (2000; 2006) has consistently argued for the need for early intervention to prevent aggressive behaviour. His work and others has demonstrated that individuals who belong to persistent aggression trajectories throughout childhood and adolescence had their aggressive behaviour start in the second year of life. Whilst the majority of aggressive two year olds will show a normal decline in aggression with age, the existence of accompanying CU traits may help demarcate a subgroup for early intervention. The benefits of early intervention cannot be emphasised enough. There is increasing evidence for child driven effects on parenting, in that child problem behaviour evokes negative parenting which in turn increases the child's problem behaviour and negatively impacts on the parent-child relationship (Patterson, 2002). Children with problem behaviour are more likely to be rejected by their peers, show scholastic impairments and other comorbid conditions (Meltzer et al., 2003). The longer problem behaviour persists the more entrenched it becomes,

with all these factors contributing to the maintenance of the problem behaviour, and these children will then often go on to show life-course persistent problems. Early intervention not only has the potential to dramatically improve the life of the target child and their proximal social network, it also reduces the cost to society from the consequences of antisocial behaviour.

The evidence for sex differences in the associations of CU traits with aggression from 2.5 to 5 years and in mechanisms of translation of CU traits to aggression also has important implications for intervention, as these findings underscore the need to consider whether interventions are effective for both males and females. Subject to replication, the finding that low physiological reactivity is not involved in CU traits or in the translation of CU traits to aggression for females and that it is only involved in the translation of CU traits to aggression in males, directly challenge the notion that all CU traits are underpinned by fearlessness and reduced physiological arousal. Fearlessness is considered to cause insensitivity to punishment, which might directly inform the techniques employed in therapeutic interventions. The present findings suggest that adapting interventions in this way may be effective for males but not necessarily for females. If replicated, the present findings suggest the need to try and develop interventions that will be best suited to the processes underlying the translation of CU traits to aggression in females. Specifically targeting interventions to the needs of the recipient group would also likely increase engagement and compliance with treatment. Hipwell and Loeber (2006) documented a reduced willingness to engage in treatment from females with conduct problems. The development of specific targeted interventions may help overcome this barrier.

## 6.5 Overall Conclusion

The findings of this thesis have advanced our understanding of CU traits in the early childhood to early-school age period, both by replicating previously demonstrated findings and by producing some important novel contributions to the literature. A psychometrically sound CU traits measure which sampled a range of relevant behaviours was successfully created at ages 2.5, 3.5 and 5 years.Despite the

measures comprising differing items, they showed a level of stability over two and a half years which was only somewhat smaller than that found for older samples of children. CU traits at age 2.5 years showed significant cross-sectional associations with aggression in boys and girls, consistent with findings from older samples, but only showed incremental prediction to aggression in girls. Instead for boys, a very strong continuity in aggression was found, which suggested multiple directions for future research.

We also replicated the association between increased maternal warmth and decreased child CU traits found with older populations, but we are the first to show this prediction from parenting in infancy, and to demonstrate that maternal sensitivity to infant distress cues in infancy (and not to non-distress cues) predicted reduced child CU traits. Sensitivity to distress and warmth also showed a significant interaction, indicating that the combination of both may be the most beneficial to reduce child CU traits. This has important practical implications, suggesting that early interventions might also focus on enhancing maternal responsiveness to distress. This was also the first study to examine attachment in infancy assessed using the SSP and later child CU traits No evidence for an association was found and so attachment did not mediate the associations between early parenting and later child CU traits. With replication, this finding suggests that the beneficial effects of warmth and sensitivity to distress do not operate through emotion regulation with a caregiver, which is frequently assumed to be the mechanism through which parental warmth reduces child CU traits.

CU traits and aggression were also examined over the age range 5 to 7 years, which is an important developmental period where the child starts full-time education. Analyses were conducted to test for sex differences and over this age range CU traits showed equal prediction to aggression in boys and girls after accounting for initial aggression. The study was novel by testing a specific hypothesis regarding the translation of CU traits to aggressive behaviour, a question that has largely been neglected in the literature, by testing for moderation of the association between CU traits and aggression by cortisol reactivity. Consistent with predictions, reduced cortisol reactivity moderated the association between CU traits and aggression in boys, and there was no evidence for moderation in girls. The finding was consistent with a growing literature implicating reduced physiological

reactivity as a risk process for males only, but was the first to demonstrate this in relation to the translation of CU traits to aggression in boys. The study highlights the important of addressing the question of what creates the risk for aggression in the context of CU traits. The findings raise the possibility that the fearlessness pathway to CU traits may in fact be the pathway from CU traits to aggression, and in boys only. Further, the findings of this thesis underscore the importance of examining for sex differences in CU traits research wherever sample characteristics allow it. The majority of theoretical models of the development of CU traits and antisocial or aggressive behaviour were developed from males, it is essential that we ensure that these models also apply to females. And further, that we develop specific hypotheses about the processes involved in the development of CU traits and aggression in females.

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Waller, R., Shaw, D. S., Neiderhiser, J. M., Ganiban, J. M., Natsuaki, M. N., Reiss, D., et al. (2017). Toward an understanding of the role of the environment in the development of early callous behavior. *Journal of Personality, 85*(1), 90-103.

Waller, R., Wright, A. G., Shaw, D. S., Gardner, F., Dishion, T. J., Wilson, M. N., & Hyde, L. W. (2015). Factor structure and construct validity of the parent-reported Inventory of Callous-Unemotional Traits among high-risk 9-year-olds. *Assessment, 22*(5), 561-580.

Waschbusch, D. A., Carrey, N. J., Willoughby, M. T., King, S., & Andrade, B. F. (2007). Effects of methylphenidate and behavior modification on the social and academic behavior of children with disruptive behavior disorders: The

moderating role of callous/unemotional traits. *Journal of Clinical Child and Adolescent Psychology*, *36*(4), 629-644.

Willoughby, M. T., Mills-Koonce, W. R., Gottfredson, N. C., & Wagner, N. J. (2014). Measuring callous unemotional behaviors in early childhood: Factor structure and the prediction of stable aggression in middle childhood.*Journal of Psychopathology and Behavioral Assessment, 36*(1), 30-42.

Zagron, G., & Weinstock, M. (2006). Maternal adrenal hormone secretion mediates behavioural alterations induced by prenatal stress in male and female rats. *Behavioural Brain Research, 175*(2), 323-328.

Zeanah, C. H., Danis, B., Hirshberg, L., Benoit, D., Miller, D., & Scott Heller, S. (1999). Disorganized attachment associated with partner violence: A research note. *Infant Mental Health Journal, 20*(1), 77-86.

Appendix 1: Ethical approval letters

**Cheshire North & West Research Ethics Committee**
Cheshire West PCT
1829 Building
Countess of Chester Health Park
Liverpool Road
Chester
CH2 1HJ

Telephone: 01244 650 334
Facsimile: 01244 650 333

27 June 2006

Professor Jonathan Hill
Professor of Child and Developmental Psychiatry
University of Liverpool, Alder Hey Hospital
Mulberry House, Alder Hey Hospital
Eaton Road
L12 2AP

Dear Professor Hill

**Full title of study:** **The Wirral Child Health and Development Study**
**REC reference number:** **05/Q1506/107**

Thank you for your letter of 19 May 2006, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice-Chairman.

**Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

**Conditions of approval**

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

**Approved documents**

The final list of documents reviewed and approved by the Committee is as follows:

| *Document* | *Version* | *Date* |
|---|---|---|
| Application | | 09 January 2006 |
| Investigator CV | | |
| Protocol | 1 | 09 January 2006 |
| Covering Letter | | 09 January 2006 |
| Summary/Synopsis | 1 | 09 January 2006 |
| Response to Request for Further Information | | 19 May 2006 |
| Father Information Sheet, Study 1500 - Phases 1, 3, 5 & 7 | 2 | 01 May 2006 |
| Study 300 Parent Information Sheet, one year - Phase 8 | 2 | 01 May 2006 |
| Study 300 Parent Information Sheet, 6 months - Phase 6 | 2 | 01 May 2006 |

| | | |
|---|---|---|
| Study 300 Parent Information Sheet, Antenatal Phases 2 & 4 | 2 | 01 May 2006 |
| Mother Information Sheet, Study 1500 - Phases 1, 3, 5, & 7 | 2 | 01 May 2006 |
| Letter confirming funding - MRC | | 09 March 2005 |
| Supporting letter from Mr Doyle, Wirral Hospitals NHS Trust | | 09 December 2005 |
| Supporting letter from Ms Sheila Hillhouse, Birkenhead & Wallasey PCT | | 09 December 2005 |
| Phase 8: Study 300 12 month mother and baby postnatal assessments | 1 | 09 January 2006 |
| GP Letter Study 1500 | 1 | 01 January 2006 |
| GP Letter Study 300 | | 01 January 2006 |
| Parent Consent, Study 1500 - Phases 1, 3, 5 & 7 | 1 | 09 January 2006 |
| Consent to contact a relative - Study 1500 | 1 | 09 January 2006 |
| Parent Consent, Fathers, - Study 1500 - Phases 1, 3, 5 & 7 | 1 | 09 January 2006 |
| Parent Consent - Study 300 Antenatal, perinatal - (Phases 2 & 4) | 1 | 09 January 2006 |
| Study 300 Parent Information Sheet 6 months (Phase 6) | 1 | 09 January 2006 |
| Parent Consent - Study 300, first birthday (Phase 8) | 1 | 09 January 2006 |
| Parent Consent - Study 300, DNA First Birthday (Phase 8) | 1 | 09 January 2006 |
| Phase 1: Study 1500 mother antenatal screen | 1 | 09 January 2006 |
| Phase 1: Study 1500 father antenatal screen | 1 | 09 January 2006 |
| Phase 2: Study 300 mother antenatal interview | 1 | 09 January 2006 |
| Phase 3: Study 1500 pregnancy/obstetric/birth outcomes | 1 | 09 January 2006 |
| Phase 4: Study 300 perinatal baby assessment | 1 | 09 January 2006 |
| Phase 5; Study 1500 6-8 week questionnaire mother | 1 | 09 January 2006 |
| Phase 6: Study 300 6 month postnatal assessments mother and baby | 1 | 09 January 2006 |
| Phase 7: Study 1500 8 month questionnaire and routine health visitor developmental check (mother) | 1 | 09 January 2006 |
| Phase 7: Study 1500 8 month questionnaire (father) | 1 | 09 January 2006 |

**Research governance approval**

The study should not commence at any NHS site until the local Principal Investigator has obtained final research governance approval from the R&D Department for the relevant NHS care organisation.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

NHS
National Research Ethics Service

**Cheshire Research Ethics Committee**
Western Cheshire PCT
1829 Building
Countess of Chester Health Park
Liverpool Road
Chester
CH2 1HJ

Tel: 01244 650334
Fax: 01244 650333

20 July 2007

Professor Jonathan Hill
Professor of Child and Developmental Psychiatry
Mulberry House, Alder Hey Hospital
Eaton Road
LIVERPOOL
L12 2AP

Dear Professor Hill

**Study title:** **The Wirral Child Health and Development Study**
**REC reference:** **05/Q1506/107**
**Amendment number:** **1**
**Amendment date:** **31 May 07**

The above amendment was reviewed at the meeting of the Sub-Committee of the REC held on 18 July 2007.

**Ethical opinion**

The members of the Committee present gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

**Approved documents**

The documents reviewed and approved at the meeting were:

| Document | Version | Date |
|---|---|---|
| Notice of Substantial Amendment (non-CTIMPs) | 1 | 31 May 2007 |

**Membership of the Committee**

The members of the Committee who were present at the meeting are listed on the attached sheet.

**R&D approval**

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

| 05/Q1506/107: | **Please quote this number on all correspondence** |
|---|---|

Yours sincerely

**Mr Robert Emmett**
**Committee Co-ordinator**

E-mail: rob.emmett@wcheshirepct.nhs.uk

Enclosures List of names and professions of members who were present at the meeting and those who submitted written comments

National Research Ethics Service
Cheshire Research Ethics Committee

Research Ethics Office
Victoria Building
Bishop Goss Complex
Rose Place
Liverpool
L3 3AN

Tel: 0151 330 2070
Fax: 0151 330 2075

24 March 2009

Professor Jonathan Hill
Professor of Child and Developmental Psychiatry
Mulberry House,
Alder Hey Hospital
Eaton Road
L12 2AP

Dear Professor Hill

**Study title:** **The Wirral Child Health and Development Study**
**REC reference:** **05/Q1506/107**
**Amendment number:** **2**
**Amendment date:** **12 February 2009**

The above amendment was reviewed at the meeting of the Sub-Committee of the REC held on 11 March 2009.

**Ethical opinion**

The members of the Committee present gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

**Approved documents**

The documents reviewed and approved at the meeting were:

| Document | Version | Date |
|---|---|---|
| Questionnaire | 2 | 12 February 2009 |
| Questionnaire | 2 | 12 February 2009 |
| Protocol | 3 | 12 February 2009 |
| Participant Information Sheet | 4 | 12 February 2009 |
| Participant Consent Form | 4 | 12 February 2009 |
| Participant Consent Form: future contacts | 1 | 12 February 2009 |
| Notice of Substantial Amendment (non-CTIMPs) | | 12 February 2009 |

**Membership of the Committee**

The members of the Committee who were present at the meeting are listed on the attached sheet.

**R&D approval**

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

| 05/Q1506/107: | **Please quote this number on all correspondence** |
|---|---|

Yours sincerely

pp

**Mr Robert Emmett**
**Committee Co-ordinator**

E-mail: rob.emmett@liverpoolpct.nhs.uk

Enclosures — List of names and professions of members who were present at the meeting and those who submitted written comments

L13

NHS

**National Research Ethics Service**

***North West 5 Research Ethics Committee - Haydock Park***

North West Centre for Research Ethics Committees
3rd Floor - Barlow House
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7819
Facsimile: 0161 237 9427

07 June 2010

**Professor J Hill**
**Professor of Child & Adolescent Psychiatry**
**Room 4.321 Jean McFarlane Building**
**The University of Manchester**
**Oxford Road**
**MANCHESTER M13 9PL**

Dear Professor Hill

| | |
|---|---|
| ***Full title of study:*** | **Social, emotional & biological processes in emergent conduct disorders: The Wirral Child Health and Development Study 1-4 years** |
| ***REC reference number:*** | **10/H1010/4** |

Thank you for your letter of 08 May 2010, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by Professor Caroline Carlisle (Professor of Education, Nursing and Midwifery).

**Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

**Ethical review of research sites**

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. I will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.

**Conditions of the favourable opinion**

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

For NHS research sites only, management permission for research ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk. *Where the only involvement of the NHS organisation is as a Participant Identification Centre, management permission for research is not required but the R&D office should be notified of the study. Guidance should be sought from the R&D office where necessary.*

*Sponsors are not required to notify the Committee of approvals from host organisations.*

**It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

**Approved documents**

The final list of documents reviewed and approved by the Committee is as follows:

| *Document* | *Version* | *Date* |
|---|---|---|
| Covering Letter - from Dr Helen Sharp, Chartered Consultant Clinical Psychologist and Lecturer in Clinical Child and Adolescent Psychology, University of Liverpool | | 22 February 2010 |
| REC application | IRAS Version 2.5 | 22 February 2010 |
| Protocol | 1 | 22 February 2010 |
| Ethical issues and Safety Protocol | 1 | 22 February 2010 |
| Investigator CV - for Professor Jonathan Hill | | 22 February 2010 |
| Investigator CV - for Dr Helen Sharp | | 22 February 2010 |
| Participant Consent Form: Phases 10/12 - Mother | 1 | February 2010 |
| Participant Consent Form: Phases 10/12 - Partner | 1 | February 2010 |
| Participant Consent Form: Phases 10/12 - Guardian | 1 | February 2010 |
| Participant Consent Form: Phase 10 - Mother - DNA analysis | 1 | February 2010 |
| Participant Consent Form: Phases 9,11,12 - Mother - Intensive | 1 | February 2010 |
| Participant Consent Form: Phases 9,11,12 - Guardian - Intensive | 1 | February 2010 |
| Participant Consent Form: Phase 9 - Mother - DNA analysis | 1 | February 2010 |
| Participant Consent Form: Phases 9,11 - Mother - Infant RNA | 1 | February 2010 |
| Participant Consent Form: Parent - Study 300 GP tracking (previously approved by Cheshire LREC) | 1 | May 2007 |
| Participant Consent Form: for future contacts (previously approved by Cheshire LREC) | 1 | February 2010 |
| Participant Consent Form: to contact a relative - extensive sample | 1 | |
| Letter to GP and Health Visitor - Extensive/Intensive Study | 1 | February 2010 |
| Health Visiting Team contact form | 1 | 22 February 2010 |
| Evidence of insurance or indemnity: Letter from Mohammed Zubair, Faculty Research Practice Co-ordinator, The University of Manchester | | 22 February 2010 |
| Pan-Manchester R&D Notification Form | | 22 July 2009 |

NHS
Health Research Authority
National Research Ethics Service

**NRES Committee North West - Haydock**
North West Centre for Research Ethics Committees
3rd Floor - Barlow House
4 Minshull Street
Manchester
M1 3DZ

Tel: 0161 625 7819/7832
Fax: 0161 237 9427

30 May 2012

**Dr Helen Sharp**
**Senior Lecturer in Clinical Psychology**
**Consultant Clinical Psychologist**
**Division of Clinical Psychology**
**Whelan Building**
**University of Liverpool**
**Brownlow Hill**
**Liverpool L69 3GB**

Dear Dr Sharp

| | |
|---|---|
| **Study title:** | **Social, emotional & biological processes in emergent conduct disorders: The Wirral Child Health and Development Study 1-4 years** |
| **REC reference:** | **10/H1010/4** |
| **Amendment number:** | **Amendment 1** |
| **Amendment date:** | **22 May 2012** |

The above amendment was reviewed at the meeting of the Sub-Committee held on 29 May 2012.

**Ethical opinion**

The amendment (Amendment 1: 22 May 2012) aims to enhance the measurement of (I) child physiological responding in the study (II) adult functioning and (III) adult report on child development. This will be done by changes to some of the specific questionnaires, interviews and physiological recordings made in phases 11 and 12 of the longitudinal study. The amendment also seeks to inform the ethics committee that some of the biological samples of saliva held for DNA and RNA analysis currently held by the study in Institute of Psychiatry in London will now be stored and analysed in the University of Liverpool, Department of Pharmacology samples bank.

A comprehensive, clear and well written rationale had been submitted in support of the amendment.

The Sub-Committee identified no ethical issues with the proposed amendment.

**The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.**

**Approved documents**

The documents reviewed and approved at the meeting were:

| Document | Version | Date |
|---|---|---|
| Notice of Substantial Amendment (non-CTIMPs) | Amendment 1 | 22 May 2012 |
| Protocol | Version 2 WCHADS 1-4 Protocol | 22 May 2012 |
| Participant Consent Form: F 220512 Intensive sample consent phases 9,11,12 | 2 | 22 May 2012 |
| Participant Information Sheet: F 220512 Phase 9, 11, 12 Intensive sample participant information sheet | 2 | 22 May 2012 |
| Participant Consent Form: F 220512 Phase 10 and 12 mother consent | 2 | 22 May 2012 |
| Participant Consent Form: F 220512 Consent for GP or health care provider tracking in future | 2 | 22 May 2012 |
| Participant Consent Form: F 220512 Phase 9, 10 and 11 DNA consent form | 2 | 22 May 2012 |
| Participant Information Sheet: F 220512 Final phase 10 and 11 extensive sample mother participant information sheet | 2 | 22 May 2012 |
| A1 Irritable or withdrawn behaviours | 1 | 22 May 2012 |
| A2 cesd-depression-test | 1 | 22 May 2012 |
| A3 SAM aggression interview questions | 1 | 22 May 2012 |
| A4 MMEA scale- multidimensional measure of emotional abuse | 1 | 22 May 2012 |
| A5 Dyadic adjustment Scale Your relationship with your partner | 1 | 22 May 2012 |
| A6 DEEP Emotional Expression in Relationships | 1 | 22 May 2012 |
| A7 Head injury questions | 1 | 22 May 2012 |
| A8 Adapted parental cognitions scale | 1 | 22 May 2012 |
| A9 Snack delay | 1 | 22 May 2012 |
| A10 Spin the pots and tower of cardiff task | 1 | 22 May 2012 |
| A11 BIS-Parent version Scale | 1 | 22 May 2012 |
| A12 SDQ_English(UK)_pt4-16single | 1 | 22 May 2012 |
| A13 Alabama Parenting Scale | 1 | 22 May 2012 |
| A14 chaos scale - short form | 1 | 22 May 2012 |
| A15 SRP III with empathy items | 1 | 22 May 2012 |
| A16 Empathy – researcher hurts his/her finger | 1 | 22 May 2012 |
| A17 Empathy – baby crying | 1 | 22 May 2012 |
| A18 Penny Hiding | 1 | 22 May 2012 |
| A19 Schultz Test of Emotion Processing—Preliminary Version | 1 | 22 May 2012 |
| A20 Simulated argument paradigm | 1 | 22 May 2012 |
| A21 Connors Kidde Continuous performance test version 5 | 1 | 22 May 2012 |

| | | |
|---|---|---|
| A22 Electrodermal skin conductance Biopac GSR100C | 1 | 22 May 2012 |
| A23 Galvanic skin response photo | 1 | 22 May 2012 |
| A24 Edinburgh Handedness Measure | 1 | 22 May 2012 |
| A25 BioImpedence Cardiography 220512 | 1 | 22 May 2012 |
| A26 BIOPAC equipment certification | | 09 May 2012 |

**Membership of the Committee**

The members of the Committee who took part in the review are listed on the attached sheet.

**R&D approval**

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

| | |
|---|---|
| **10/H1010/4:** | **Please quote this number on all correspondence** |

Yours sincerely

*On behalf of*-

**Professor Ravi S Gulati**
**Chair**

**E-mail:** noel.graham@northwest.nhs.uk

**Enclosures:** List of names and professions of members who took part in the review

A Research Ethics Committee established by the Health Research Authority

Health Research Authority
National Research Ethics Service

**NRES Committee North West - Haydock**
HRA NRES Centre - Manchester
3rd Floor - Barlow House
4 Minshull Street
Manchester
M1 3DZ

Tel: 0161 625 7827
Fax: 0161 625 7299

20 May 2013

**Professor Jonathan Hill**
**University of Manchester**
**Oxford Road**
**Manchester**
**M13 9PL**

Dear Professor Hill

| | |
|---|---|
| **Study title:** | **Social, emotional & biological processes in emergent conduct disorders: The Wirral Child Health and Development Study 1-4 years** |
| **REC reference:** | **10/H1010/4** |
| **Amendment number:** | **Amendment 2 29/4/13** |
| **Amendment date:** | **30 April 2013** |
| **IRAS project ID:** | **42529** |

The above amendment was reviewed at the meeting of the Sub-Committee held on 14 May 2013.

**Ethical opinion**

The amendment sought approval to add a teacher measure of school readiness to the measures, as well as for asking teachers for information about child development. Furthermore, permission was sought to use still images and video material.

The Sub-Committee identified no ethical issues with the proposed amendment.

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

**Approved documents**

The documents reviewed and approved at the meeting were:

| Document | Version | Date |
|---|---|---|
| Head teacher letter- phases 11, 12 | 1 | 01 April 2013 |
| Parent Letter about School Skills Survey- phases 11, 12 | 1 | |
| Griffiths Empathy Scale | | |

| | | |
|---|---|---|
| Teacher Questionnaire | | |
| Parent Questionnaire | | |
| Participant Consent Form: Mother Consent- Recordings | 1 | 01 April 2013 |
| Research Consent Form Parent | 1 | 01 April 2013 |
| Protocol tracked | | |
| Notice of Substantial Amendment (non-CTIMPs) | 2 | 29 April 2013 |

**Membership of the Committee**

The members of the Committee who took part in the review are listed on the attached sheet.

**R&D approval**

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

| | |
|---|---|
| **10/H1010/4:** | **Please quote this number on all correspondence** |

Yours sincerely

On behalf of
**Professor Ravi S Gulati**
**Chair**

**Email:** nrescommittee.northwest-haydock@nhs.net

**Enclosures:** List of names and professions of members who took part in the review

**Copy to:** Dr Will Sopwith
NHS Wirral (Wirral PCT)

Mr Mohammed Zubair
University of Manchester

**NRES Committee North West - Haydock**

**Attendance at Sub-Committee of the REC meeting on 14 May 2013**

| *Name* | *Profession* | *Capacity* |
|---|---|---|
| Mr Stephen Edgar | Designer | Lay Plus |
| Dr Michael U Eshlett | Consultant Physician in Neurological Rehabilitation | Expert |
| Professor Ravi S Gulati | Consultant Physician | Expert |
| Ms Pat Harvey | Hospital Chaplain | Lay Plus |
| Mrs Chris Haywood | Nurse & Head of Hospice Services | Expert |
| Mr Charles Otim | Research Support Officer | Lay Plus |
| Dr David Pilling | Consultant Radiologist | Expert |
| Dr Valerie E Siddall | Retired Senior Manager - Pharmaceutical Industry | Lay Plus |
| Dr Tim S Sprosen | Epidemiologist | Expert |
| Mr Peter Ward | Lay Member | Lay |

**Also in attendance:**

| *Name* | *Position (or reason for attending)* |
|---|---|
| Ms Josephine Foxall Dant | Assistant Committee Co-ordinator |
| Mrs Rinat Jibil | REC Coordinator |

NHS
Health Research Authority
National Research Ethics Service

**NRES Committee North West - Haydock**
3rd Floor - Barlow House
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7827
Fax: 0161 625 7299

22 December 2014

Professor Jonathan Hill
Professor of Child & Adolescent Psychiatry
University of Reading
School of Psychology and Clinical Language Sciences
White Knights
Reading
RG6 6AL

Dear Professor Hill

| | |
|---|---|
| **Study title:** | **The Wirral Child Health and Development Study 7-9 years: Prenatal and infancy origins of biological and social-cognitive processes in disruptive behaviour problems in children.** |
| **REC reference:** | **14/NW/1484** |
| **IRAS project ID:** | **165660** |

Thank you for your submission of 18 December 2014, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by Alternate Vice-Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager, Rachel Katzenellenbogen, nrescommittee.northwest-haydock@nhs.net. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

**Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

**Conditions of the favourable opinion**

The favourable opinion is subject to the following conditions being met prior to the start of the

study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from NRES. Guidance on where to register is provided on the HRA website.

**It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

**Ethical review of research sites**

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

**Approved documents**

The final list of documents reviewed and approved by the Committee is as follows:

| Document | Version | Date |
|---|---|---|
| Covering letter on headed paper [F WCHADS 7-9 1 Covering letter to ethics committee] | 1 | 26 November 2014 |
| Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Indemnity Certificate] | 1 | 24 November 2014 |
| GP/consultant information sheets or letters [WCHADS 7-9 letter to | 1 | 28 October 2014 |

| | | |
|---|---|---|
| GP to inform them of participation] | | |
| Instructions for use of medical device [RSA and skin conductance measurement] | 1 | 28 October 2014 |
| Instructions for use of medical device [ Saliva collection for cortisol analysis procedure] | 1 | 28 October 2014 |
| Instructions for use of medical device [Saliva collection for DNA testing] | | 28 October 2014 |
| Interview schedules or topic guides for participants [Integrated maternal interview] | 1 | 28 October 2014 |
| Letter from funder [proof of MRC grant funding WCHADS7-9] | 1 | 11 April 2014 |
| Letter from sponsor [Sponsorship letter] | 1 | 24 November 2014 |
| Non-validated questionnaire [WCHADS 7-9 Demographic, Health and lifestyle update 281014] | 1 | 28 October 2014 |
| Other [WCHADS 7-9 3 Ethical issues and safety protocol 281014] | 1 | 28 October 2014 |
| Other [WCHADS 7-9 281014 Age 7 Letter to Headteachers] | 1 | 28 October 2014 |
| Other [WCHADS 7-9 281014 Age 9 Letter to Headteachers] | 1 | 28 October 2014 |
| Other [Edinburgh Handedness Measure] | | |
| Other [Developmental / observational assessment: Child growth measurement] | 1 | 28 October 2014 |
| Other [Mother-child Observational Assessment] | 1 | 28 October 2014 |
| Other [Affective and physiological arousal to picture and sound stimuli] | 1 | 28 October 2014 |
| Other [Social inclusion-exclusion paradigm] | 1 | 28 October 2014 |
| Other [Schultz Test of Emotion Processing] | 1 | 28 October 2014 |
| Other [Empathy and Theory of Mind] | 1 | 28 October 2014 |
| Other [Cognitive and Executive Functioning tasks] | 1 | 28 October 2014 |
| Other [Emotion Recognition with Eye Gaze – emotion matching and labelling] | 1 | 28 October 2014 |
| Other [Covering letter to ethics committee following provisional response on 9th December] | 1 | 16 December 2014 |
| Participant consent form [Extensive sample consent mother phases 13 and 14] | 1 | 28 October 2014 |
| Participant consent form [Intensive sample consent phases 13 and 14] | 1 | 28 October 2014 |
| Participant consent form [Phase 13 DNA consent form] | 1 | 28 October 2014 |
| Participant consent form [Phase 13, 14 Consent for Contacting School] | 1 | 28 October 2014 |
| Participant consent form [Consent form for use of DVD recordings and still images] | 1 | 28 October 2014 |
| Participant consent form [Consent for GP or health care provider tracking in future] | 1 | 28 October 2014 |
| Participant consent form [WCHADS 1-4 Feb 09 Extensive sample Consent form for future contacts mother] | | 01 February 2009 |
| Participant consent form [WCHADS 1-4 220512 Consent for GP or health care provider tracking in future] | | 22 May 2012 |
| Participant consent form [Extensive and Intensive Sample consent form - partner version] | 2 | 16 December 2014 |
| Participant information sheet (PIS) [F WCHADS 7-9 281014 V1R Extensive sample Phase13-14 Participant Information Sheet mother ] | 1 | 28 October 2014 |
| Participant information sheet (PIS) [F WCHADS 7-9 281014 V1R Phase 13 and 14 Intensive sample participant information sheet] | 1 | 28 October 2014 |
| Participant information sheet (PIS) [Extensive and Intensive sample Phase13-14 Participant Information Sheet partner] | 2 | 16 December 2014 |
| REC Application Form [REC_Form_25112014] | | 25 November 2014 |
| Referee's report or other scientific critique report [Referee 1 | | 06 January 2014 |

| | | |
|---|---|---|
| comments] | | |
| Referee's report or other scientific critique report [Referee 2 comments] | | 12 January 2014 |
| Referee's report or other scientific critique report [Referee 3 comments] | | 20 January 2014 |
| Referee's report or other scientific critique report [Applicants reply to referee comments] | 1 | |
| Research protocol or project proposal | 1 | 28 October 2014 |
| Summary CV for Chief Investigator (CI) [CV J Hill] | 1 | 28 October 2014 |
| Summary, synopsis or diagram (flowchart) of protocol in non technical language [Table summarising measures in WCHADS 7-9] | 1 | 28 October 2014 |
| Validated questionnaire [Center for Epidemiologic Studies Depression Scale (CES-D)] | | |
| Validated questionnaire [General Health Questionnaire-12] | | |
| Validated questionnaire [Spielberger State&"Trait Anxiety Inventory] | | |
| Validated questionnaire [Kansas Marital Satisfaction Scale] | | |
| Validated questionnaire [Inventory of Callous Unemotional traits] | | |
| Validated questionnaire [The PCLC – my response to stress] | | |
| Validated questionnaire [Dunedin Relationship Scale - Psychological] | | |
| Validated questionnaire [Dunedin Relationship scale -Physical Abuse] | | |
| Validated questionnaire [Child Behaviour Checklist (CBCL, 6 – 18 years)] | | |
| Validated questionnaire [Parent report Ballargeon Peer aggression Scale - parent] | | |
| Validated questionnaire [Ballargeon Peer aggression Scale - child] | | |
| Validated questionnaire [Parental Feelings Questionnaire ] | | |
| Validated questionnaire [Reactive-proactive aggression behaviour] | | |
| Validated questionnaire [Dyadic Adjustment Scale] | | |
| Validated questionnaire [Dyadic Adjustment Scale- short form] | | |
| Validated questionnaire [Parental cognitions scale] | | |
| Validated questionnaire [Strengths and Difficulties Questionnaire] | | |
| Validated questionnaire [Alabama Parenting Questionnaire] | | |
| Validated questionnaire [Behavioural Inhibition Scale] | | |
| Validated questionnaire [Irritable withdrawn behaviours] | | |
| Validated questionnaire [Chaos scale – short form] | | |
| Validated questionnaire [Antisocial Process Screening Device - 6 item subscale assessing callous unemotional traits.] | | |
| Validated questionnaire [Connor's short form] | | |
| Validated questionnaire [Social Communication Questionnaire] | | |
| Validated questionnaire [Griffiths Empathy Scale] | | |
| Validated questionnaire [parent - Observations of Attachment behaviours ] | | |
| Validated questionnaire [Autism Quotient] | | |
| Validated questionnaire [Teacher - Observations of Attachment behaviours ] | | |
| Validated questionnaire [Teacher Report Form – (CBCL 6-18 years)] | | |
| Validated questionnaire [Teacher APSD And prosocial SDQ items] | | |
| Validated questionnaire [Student-teacher relationship scale] | | |
| Validated questionnaire [Macarthur Health and Behaviour Questionnaire] | | |

| | | |
|---|---|---|
| Validated questionnaire [teacher report - Reactive - proactive aggression ] | | |
| Validated questionnaire [Peer conflict scale – child report] | | |
| Validated questionnaire [Friendship interview - child] | | |
| Validated questionnaire [Adult-Adolescent Parenting Inventory – empathy scale] | 2 | 16 December 2014 |

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

**After ethical review**

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

**User Feedback**

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

**HRA Training**

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

| | |
|---|---|
| **14/NW/1484** | **Please quote this number on all correspondence** |

With the Committee's best wishes for the success of this project.

Yours sincerely

**On behalf of**

NHS
Health Research Authority

North West - Haydock Research Ethics Committee
3rd Floor - Barlow House
4 Minshull Street
Manchester
M1 3DZ

Tel: 0207 104 8001

28 April 2016

Professor Jonathan Hill
Professor of Child & Adolescent Psychiatry
University of Reading
School of Psychology and Clinical Language Sciences
White Knights
Reading
RG6 6AL

Dear Jonathan

| | |
|---|---|
| **Study title:** | **The Wirral Child Health and Development Study 7-9 years: Prenatal and infancy origins of biological and social-cognitive processes in disruptive behaviour problems in children.** |
| **REC reference:** | **14/NW/1484** |
| **Amendment number:** | **Amendment 1** |
| **Amendment date:** | **01 February 2016** |
| **IRAS project ID:** | **165660** |

The above amendment was reviewed at the meeting of the Sub-Committee held on 26 April 2016 by the Sub-Committee.

**Favourable opinion**

Approval was sought for additional questions in the questionnaires as well as for changes to the Participant Information Sheet, consent forms and protocol. Approval was also sought to store data and conduct analysis at Manchester Metropolitan University

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

**Approved documents**

The documents reviewed and approved at the meeting were:

| Document | Version | Date |
|---|---|---|
| Non-validated questionnaire [7-9 Child Eating Behaviour Questionnaire] | 1 | 01 February 2016 |
| Non-validated questionnaire [Inventory of Callous-Unemotional | Version 1 | 28 October 2014 |

| | | |
|---|---|---|
| Traits] | | |
| Notice of Substantial Amendment (non-CTIMP) | Amendment 1 | 01 February 2016 |
| Participant consent form [Research Consent Form Tracked] | 2 Feb 2016 | 02 February 2016 |
| Participant consent form [V2R Intensive sample consent phases 13-14] | 2 Feb 2016 | 02 February 2016 |
| Participant consent form [Research Consent for DNA Analysis] | 2 Feb 2016 | 02 February 2016 |
| Participant consent form [V2R Phase 13, 14 Consent for Contacting School] | 2 Feb 2016 | 02 February 2016 |
| Participant consent form [v3 Consent for GP or health care provider tracking in future] | 2 Feb 2016 | 02 February 2016 |
| Participant consent form [v3 Extensive and intensive sample consent partner Phase 13 and 14] | 2 Feb 2016 | 02 February 2016 |
| Participant information sheet (PIS) [Extensive sample Phase 13-14 PIS mother] | 2 Feb 2016 | 02 February 2016 |
| Participant information sheet (PIS) [V2R Phase 13 and 14 Intensive sample PIS ] | 2 Feb 2016 | 02 February 2016 |
| Participant information sheet (PIS) [V3R Phase 13-14 PIS partner] | 3 February 2016 | 02 February 2016 |
| Research protocol or project proposal | 2 | 01 February 2016 |

**Membership of the Committee**

The members of the Committee who took part in the review are listed on the attached sheet.

**R&D approval**

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

| | |
|---|---|
| **14/NW/1484:** | **Please quote this number on all correspondence** |

Yours sincerely

**Dr Tim S Sprosen**
**Chair**

E-mail: nrescommittee.northwest-haydock@nhs.net

Enclosures: List of names and professions of members who took part in the

North West - Haydock Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 26 April 2016

Committee Members:

| Name | Profession | Present | Notes |
|---|---|---|---|
| Dr Valerie E Siddall | Retired Senior Manager - Pharmaceutical Industry | Yes | |
| Dr Tim S Sprosen | Epidemiologist | Yes | |

Also in attendance:

| Name | Position (or reason for attending) |
|---|---|
| Ms Rachel Katzenellenbogen | REC Manager |

NHS
Health Research Authority

North West - Haydock Research Ethics Committee
3rd Floor - Barlow House
4 Minshull Street
Manchester
M1 3DZ

Tel: 0207 104 8004

**Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.**

10 April 2017

Dr Helen Sharp PhD DClinPsy
Consultant Clinical Psychologist
Department of Psychological Science
Institute of Psychology, Health and Society
Whelan Building
University of Liverpool
Brownlow Hill
Liverpool
L69 3GB

Dear Helen,

| | |
|---|---|
| **Study title:** | **The Wirral Child Health and Development Study 7-9 years: Prenatal and infancy origins of biological and social-cognitive processes in disruptive behaviour problems in children.** |
| **REC reference:** | **14/NW/1484** |
| **Amendment number:** | **2** |
| **Amendment date:** | **13 March 2017** |
| **IRAS project ID:** | **165660** |

The above amendment was reviewed by the Sub-Committee in correspondence.

**Favourable opinion**

This amendment consisted of submitting new questionnaires to understand how early life stress may contribute to social, emotional and behavioural problems during childhood.

No material ethical issues were raised.

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

**Approved documents**

The documents reviewed and approved at the meeting were:

| Document | Version | Date |
|---|---|---|
| Interview schedules or topic guides for participants [Friendship interview - child report] | 1 | 13 March 2017 |
| Non-validated questionnaire [The Family Questionnaire - parent report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Life events checklist - parent report Tracked] | 2 | 13 March 2017 |
| Non-validated questionnaire [GAD 7 - parent report ] | 1 | 13 March 2017 |
| Non-validated questionnaire [Parental Bonding Instrument - Parent report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Patient Health Questionnaire - depression parent report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Pubertal Development Scale - Parent report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Kansas Marital Satisfaction Scale - parent report Tracked] | 2 | 13 March 2017 |
| Non-validated questionnaire [Free time activities - child report ] | 1 | 13 March 2017 |
| Non-validated questionnaire [Nisonger self-harm subscale - parent report ] | 1 | 13 March 2017 |
| Non-validated questionnaire [Demographic Health and lifestyle update - parent report] | 14 | 13 March 2017 |
| Non-validated questionnaire [Borderline Personality Disorder Features Scale - child report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Borderline Personality Disorder Features Scale - parent report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Free time activities and sleep - parent report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Physical Activity Questionnaire - child report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Friendship Qualities Measure - child report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Illinois Bully Scale - child report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Childrens Social Behaviour Scale - Child Self-report] | 1 | 13 March 2017 |
| Non-validated questionnaire [Forms of Bullying Questionnaire - child report] | 1 | 13 March 2017 |
| Notice of Substantial Amendment (non-CTIMP) | 2 | 13 March 2017 |
| Other [Child Growth Measurements Tracked] | 2 | 13 March 2017 |
| Other [Modified Cyberball with social support ] | 1 | 13 March 2017 |
| Other [Trust Game] | 1 | 13 March 2017 |
| Other [Cognitive and Executive functioning tasks] | 1 | 13 March 2017 |
| Other [Mother child observational procedure] | 1 | 13 March 2017 |
| Participant consent form [Intensive Mother - consent for phase 14] | 1 | 13 March 2017 |
| Participant consent form [Extensive sample - Consent for phase 14] | 1 | 13 March 2017 |
| Participant information sheet (PIS) [ Intensive Mother Phase 13 and | 3 | 13 March 2017 |

Appendix 2- Participant information sheets
**Phase 1, 3, 5, and 7 extensive**

Version 3. March 2007 Mother Information Sheet, Study 1500 – Phases 1,3,5 &7

MANCHESTER 1824

The University of Manchester

Wirral University Teaching Hospital NHS
NHS Foundation Trust

UNIVERSITY OF LIVERPOOL


**Study Base:**
**The Lauries Centre, 142 Claughton Road,**
**Birkenhead, Wirral, CH41 6EY**
**Freephone: 0800 051 7597**
**(from a mobile) 800 051 7597**
**Text: 07956 297412**

**Parent Information Sheet (Mother)– Study 1500**

**Title of study : The Wirral Child Health and Development Study**

**Investigators: Jonathan Hill, Helen Sharp, Andrew Pickles, Gill Lancaster**
**Research Staff: Karen Lunt, Carol Bedwell, Belinda Thompson, Julie Carlisle, Kate Marks, Kate Marshall,Liz Green, Florin Tibu, Jo Roberts, Jenny Lee, Nichaela Broyden, Carol Sadler, Jeanette Appleton**

You are being invited to take part in a research study. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part. Thank you for reading this.

**What is the study about?**
We would like to invite you to participate in a new study of children's early development from birth to their first birthdays. This study is based at the Universities of Liverpool and Manchester. It is part of a programme of research into how children learn how to behave with other people, and why some children have difficulties controlling their behaviours. In order to fully understand this we need to measure the early development of children in many different ways. The aim of the study is to find out about the effects of many different forms of stress on parents and babies during the antenatal period and in the first months after birth. We know that for some parents and children the effects are quite long lasting, and others find ways of coping. We want to understand these processes better so that services to support families experiencing stress can be improved.

**Who is being invited to take part?**
We are approaching all first time mothers and their partners who are booked into the antenatal clinic at Arrowe Park Hospital over a two year period. It is important that we have participants in the study with low, medium and high levels of stress. If you have agreed to take this letter home a research midwife will contact you at your 20 week appointment or slightly after, to tell you more about the study, answer any questions you have and to invite you to take part.

**Do I have to take part?**
It will be up to you to decide whether or not you would like to take part. If you agree, and change your mind later, you can withdraw from the study. This will not affect the care you receive.

**How often will I be contacted?**
We will contact you again six weeks after the birth of your baby, and when your baby is 8 months old. We would also like to contact some mothers more often up to the first birthdays of their children, so that we can ask them more about their lives, and understand better their ways of coping, and assess their babies' health and development in more detail. If you decide to take part, the computer will tell us who to invite for the additional contacts after we have entered the information you provide now. If your name does come up we hope very much that you will be able to help us, but at this stage we are only asking you to participate now and at 6 weeks and eight months.

**What will I be asked to do at each time point?**
During your pregnancy we will interview you and ask you to complete some questionnaires about your current health and relationships, and about your expectations of the baby and being a mother. This can be done here at the antenatal clinic or at another clinic on the Wirral or at the study base in the Lauries Centre. It should take about 25 minutes.

We will also ask you for consent for us to have access to your medical records for the pregnancy, the birth, and your new born infant following the birth.

When your baby is 6 weeks old we will send you some short questionnaires about your health, your relationships, and about your baby by post, and ask you to 'Freepost' them back to us.

When your baby is 8 months old we will send you more questionnaires about your health and about your baby, and ask you to return them 'Freepost' to us or return them to your health visitor when you attend for your baby's routine 8 month developmental check-up. We will also ask your health visitor for the results of their 9-12 month assessment of your baby's development.

If you give written consent to take part in this study and you are selected by the computer to be invited for additional contacts, one of the research team named on the front of this information sheet will contact you at home, using the contact details you give to the research midwife. They will only contact you if you agree to it.

**How will this information be used?**
All information that we receive from you will be treated as strictly confidential, under the guidelines of the Universities of Liverpool and Manchester, the UK Medical Research Council, and the Data Protection Act. Information that we enter on the computer will be identified only by a number. We will report general findings about parents and children, but you or your child will never be identified. The only reason we might have to share information from the study with other people is if there are concerns about you or a child being at risk of serious harm. If that happens we will talk with you first to decide on the best way forward. Concerns like this would be addressed by seeking appropriate forms of help for you and/or following Trust Child Protection Guidelines.

**Who is organising and funding the research study?**
The study is being run by Professor Jonathan Hill of the University of Manchester and Dr Helen Sharp of the University of Liverpool. The research is funded by the Medical Research Council.

**Are there any benefits in taking part in this study?**
There are no benefits to you or your child's health in taking part in this study. However we hope that you will feel you are contributing to medical research in a way that will help children and families in the future.

**What if something goes wrong?**
If you feel you or your child have been harmed by taking part in this research and that the researchers have been negligent or at fault, then you may be able to make a legal claim for compensation to their employer. You might have to pay the legal costs of doing this. However, if you are harmed and the researchers are not at fault, there is no facility for you to make a claim. If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during the course of this study, normal University or National Health Service complaints procedures should be available to you.

**Are there any risks to myself or my child taking part in this study?**
No, there are no known or likely risks.

**Who has reviewed and approved the study?**
A team of international experts on child development has reviewed this study for the Medical Research Council. The study has been reviewed and approved by the Research & Development committees of Wirral Hospitals NHS Trust, Wirral PCT and the Cheshire Local Research Ethics Committee.

**Can I ask further questions?**
When the research midwife meets you, at or after your 20 week scan appointment, she will be very happy to answer any questions you might have. In the meantime, if you would like any more information, please do not hesitate to contact Professor Jonathan Hill, Dr Helen Sharp, or Liz Green on the freephone number shown on the front page.

**Appendix 2 (continued) Participant information sheet phase 10 and 12 extensive**

Study Base:
The Laurie Centre,
142 Claughton Road
Birkenhead, Wirral,
CH41 6EY
Freephone: 0800 051 7597
Text: 07956 297412

## Participant Information Sheet

**Title of study : The Wirral Child Health and Development Study 1-4 years**

**Investigators: Jonathan Hill, Helen Sharp, Andrew Pickles, John Quinn, Vivette Glover.**
**Research Staff: Liz Green, Niki Sandman, Kate Marshall, Helen Jones, Louise Fisher, Stuart Kehl, Fay Huntley, Nicky Wright, Louise Adams, Donna Yarlett, Giovanna Moretto, Rebecca Holmes.**

When you were pregnant, just after your baby was born and when your baby was 12 months old you kindly helped us with this research study. We are now inviting you to take part in this study until your first child is just over 4 years old. We have recruited 1286 families expecting their first child into this 'First Steps' study. All these mothers and many of their partners have completed questionnaire measures for us and now the children are reaching three years old. Just over 300 mothers and babies have also taken part in a more detailed part of the study in which mothers have completed a range of interviews and mother-child assessments during their child's first and second year of life. Before you decide whether you want to take part in the next stages of the study, it is important for you to understand why the research is continuing and what it will involve for you and your child. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part. Thank you for reading this.

**What is the purpose of the study?**
This study aims to find out how children learn how to behave with other people, and why some children have difficulties controlling their behaviours. To do this we need to measure many aspects of their early development, their experiences, and the ways parents take care of them. We are interested to find out more about the ways that early life stress influences later development as we know that for some parents and children the effects are quite long lasting, and others find ways of coping. Our research team is also very interested to know more about the genes that influence children's emotions and behaviours. Genes are like maps inside our bodies that hold information. We now also know that health and behaviour are influenced by genes. This information in our genes is stored in 'DNA', which can be found in our skin cells and saliva. This study provides an important opportunity to learn more about the ways in which genes and early life experiences affect the way infants behave and their ability to cope with new situations. We want to better understand all these processes so that NHS services to support families can be improved.

**Why have I been invited to take part?**
At the time when you were expecting your first child, we approached all women who were booked into the antenatal clinic at Arrowe Park Hospital for their antenatal care over a two year period. During this time we recruited 1286 mothers who were experiencing low, medium or high levels of stress in pregnancy. You were one of those mothers and we would like now to follow your child's development up to four years of age if you are happy for us to do so.

**Do I have to take part?**
It will be up to you to decide whether or not you would like to take part. If you agree, and change your mind later, you can withdraw from the study. This will not affect the care you receive.

**What will happen to me if I take part ?**
Now that your baby is around three years old we would ask our Research Health Visitor or one of their assistants to meet with you and your child at home to complete a range of assessments described below. We would also like to send some questionnaires out to you to complete again when your child is four years old. All mothers who tell us at the first visit that their child is showing behavioural difficulties at home will also be invited to join the 300 families taking part in the detailed part of the study. If you were happy to do this you would be given another information sheet and would be asked for a separate consent to complete these additional assessments. If you decide to take part we will write to your GP and your child's health visitor to inform them you have agreed to do so.

**What will we have to do?**

- One of our Research Health Visitors or their assistants would like to see you and your first child at home together for a whole morning or afternoon.
- We will ask you to complete some interviews and questionnaires about your personal circumstances, your lifestyle, recent events, relationships, your personality, emotional wellbeing and your physical health. We will ask about your first child's behaviours, physical, emotional and language development and about the parenting decisions you make on a day to day basis.
- We would like to make a short DVD (about 15 minutes) of your infant playing with you with three bags of toys we will bring with us. We will be looking at your infant's behaviours during this play time together and the different parenting skills you use.
- We would also like to collect skin cells with saliva from your baby's mouth for DNA analysis by briefly rubbing small cotton buds on the inside of your infants cheeks.
- We will ask you to consent for us to be sent a copy of your child's routine Health Visiting team assessment completed at around 2 – 2 ½ years of age.
- We will also send you a booklet of questionnaires to complete when your infant is around four years old. This will take about 45 minutes to complete. We will provide a freepost envelope for you to send it back to us.
- We wish to follow the families in the study for a long time as their children grow up and so if we get funding to do this we may ask you later to consider being in the study for longer.

For now, we are asking you to take part in this study over a two year period from when your child is about 3 years old until they are about 4 ½ years old.

**Expenses and payments**
We are able to give you £20 in high street shopping vouchers each time you complete an assessment. This is to compensate you for time lost from home or work and any other expenses incurred from taking part in the study.

**Will my taking part in the study be kept confidential?**

- Information on DVD recordings, on audio recordings of interviews with you, and on paper questionnaire records and any information we enter on computers about you will be identified only by a case number. A computer database and paper copies of participant names and addresses and contact details and their case numbers will be kept separately and securely in the university study base so no-one outside of the research team can access this or identify you or your child. All the information you give us is therefore 'pseudoanonymised' which means that it is identified ONLY by a case number and ONLY the research team will be able to link your case number to who you are and the other contact information you give us.
- We would like to make DVD recordings of your baby and you so that we go over what happened in detail afterwards. The recordings will be identified only by a case number, so that information on it cannot be traced to you by anyone outside of the research team. A copy of the recording will be kept securely at each university base for up to thirty years.
- The genetic samples will be analysed pseudo-anonymously too. This means that no records will be generated that directly link your name, your partner's name, or your child's name to the genetic samples. Instead, they will be linked only by the case number. So only the research team will know who the samples belong to. We will analyse the samples for genes that affect infants' health, emotions and behaviour, and not for any other purpose. They will not be kept as part of your medical record. All samples will be destroyed after 20 years. The pseudo-anonymous samples will be analysed by a laboratory technician who is not affiliated with the study, and will have no access to your name, your partner's name, or your child's name.
- All information that we receive from you will be treated as strictly confidential, under the guidelines of the Universities of Liverpool and Manchester, the UK Medical Research Council, and the Data

Protection Act. This means that your information will only used by members of the research team and scientific research collaborators from other academic institutions approved by us.

- We will report general research findings about parents and children, and you or your child will never be identified. Reports will be based on the ratings that we make from the interviews, questionnaires or DVD recordings and on occasions when examples of individual responses are reported these will be fully pseudo-anonymised.
- The only reason we might have to share information from the study with other people is if there are concerns about you or a child being at risk of serious harm. If that happens we will talk with you first to decide on the best way forward. Concerns like this would be addressed by seeking appropriate forms of help for you and by following Trust Child Protection Guidelines.

**What will happen to the results of the research study?**
We will publish the results of this study in academic journals, at international and national conferences and we will inform study participants of key findings in a study newsletter sent to your home. We also plan to develop a study website where results will be displayed.

**What will happen when the research study stops?**
When this part of the research comes to an end we hope to secure further funding to continue studying all the families and the children as they grow up through the school years. We would of course ask your permission to do this at a later date.

**What are the possible benefits to taking part?**
There are no benefits to you or your child's health in taking part in this study. However we hope that you will feel you are contributing to medical research in a way that will help children and families in the future.

**What are the possible disadvantages and risks to myself or my child taking part in this study?**
No, there are no known or likely risks. It is possible that you may become upset when recalling difficult experiences in your life. If this occurs the interviewer will ask you if you wish to take a break from interviewing or continue. You may also choose to stop the interview completely at any time.

**Who is organizing and funding the research ?**
The study is being led jointly by Professor Jonathan Hill of the University of Manchester and Dr Helen Sharp of the University of Liverpool. The research is funded by the Medical Research Council.

**Who has reviewed and approved the study?**
A team of international experts on child development has reviewed this study for the Medical Research Council. The study has been reviewed and approved by the Research & Development committees of Wirral Primary Care Trust and Western Cheshire Primary Care Trust and the Northwest 5 Haydock Research Ethics Committee.

**What if there is a problem?**
*Complaints*
If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If they are unable to resolve your concern or you wish to make a complaint regarding the study, please contact a University Research Practice and Governance Co-ordinator on 0161 2757583 or 0161 2758093 or by email to research-governance@manchester.ac.uk.

*Harm*
In the event that something does go wrong and you or your child are harmed during the research you may have grounds for a legal action for compensation against The University of Manchester and The University of Liverpool but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

The University of Manchester has cover for no fault compensation for bodily injury, mental injury or death where the injury resulted from a trial or procedure you received as part of the trial. This would be subject to policy terms and conditions. Any payment would be without legal commitment. (Please ask if you wish more information on this). The University would not be bound to pay this compensation where the injury resulted from a drug or procedure outside the trial protocol or the protocol was not followed.

**Further information and contact detail:**
When the researcher meets you they will be very happy to answer any questions you might have. In the meantime, if you would like any more information, please do not hesitate to contact Professor Jonathan Hill, Dr Helen Sharp or Liz Green / Niki Sandman (study administrators) on the freephone number shown on the front page.

## Appendix 2 (continued) - Participant information sheet phase 13 extensive



University of Reading


UNIVERSITY OF LIVERPOOL

Study Base:
The Laurie Centre,
142 Claughton Road
Birkenhead, Wirral,
CH41 6EY
Freephone: 0800 051 7597
(from a mobile) 800 051 7597
Text: 07956 297412

### Participant Information Sheet

**Title of study: The Wirral Child Health and Development Study 7-9 years**

**Investigators: Jonathan Hill, Helen Sharp, Andrew Pickles, John Quinn, Chris Murgatroyd.**
**Research Staff: Kay Martin, Karen Rafferty, Kate Abbott, Helen Chadwick, Louise Fisher, Stuart Kehl, Nicky Wright, Matthew Bluett-Duncan and Miriam Refberg**

When you were pregnant and during the first five years of your first child's life you have kindly helped us with this research study. We would very much like to thank you for helping us for all this time and we would like now to invite you to take part until he or she is 9 years old.

We recruited 1286 families expecting their first child into this 'First Steps' study. All these mothers and many of their partners have had a home visit at age 3-4 years and have completed questionnaire measures for us at many phases and now the children are reaching seven years old. Just over 300 mothers and children have also taken part in a more detailed part of the study in which mothers have completed a range of interviews and mother-child assessments during their child's first five years of life. Before you decide whether you want to take part in the next stages of the study, it is important for you to understand why the research is continuing and what it will involve for you and your child. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part. Thank you for reading this.

**What is the purpose of the study?**
This study aims to find out how children learn how to behave with other people as they grow up, and why some children have difficulties controlling their behaviours. To do this we need to measure many aspects of their development, their experiences at home and school, and the ways parents take care of them. We are interested to find out more about the ways that early life stress influences later development as we know that for some parents and children the effects are quite long lasting, and others find ways of coping. We know also that as children reach the school years they learn more complex ways of making sense of the world around them, so we plan to study how children understand emotions, how they think about and respond individually to social challenges. Every child is a unique individual and that is partly due to the genes that have been passed on from each parent and partly due to individual life experiences. Genes are like maps inside our bodies that hold information. We also know that health and behaviour are influenced by genes. This information in our genes is stored in 'DNA', which can be found in our saliva. We also now know that genes only influence development when they are switched on. We can tell whether genes are switched on or off at a particular time point from looking closely at the DNA. In this study we plan to collect more saliva for DNA analysis at age 7 so we can continue to monitor the activity levels of genes thought to influence behaviour and emotional responses, as children gain new life experiences. We want to find out more about how genes and different life experiences influence parent's and children's behaviours and development so that NHS and educational services that support families can be improved with this knowledge.

**Why have I been invited to take part?**
At the time when you were expecting your first child, we approached all women who were booked into the antenatal clinic at Arrowe Park Hospital for their antenatal care over a two year period. During this time we

recruited 1286 mothers who were experiencing low, medium or high levels of stress in pregnancy. You were one of those mothers and we would like now to follow your child's development up to nine years of age if you are happy for us to do so.

**Do I have to take part?**
It will be up to you to decide whether or not you would like to take part. If you agree, and change your mind later, you can withdraw from the study. This will not affect the care you receive. If you choose to take part and you find you do not wish to complete a particular assessment or answer a particular question, you will be free to miss that part out but carry on with the rest of the study if you wish or you can just choose to stop that assessment completely.

**What will happen to me if I take part ?**
Now that your child is seven years old we would like one of our research assistants to meet with you and your child at home to complete a range of assessments described below. We would also like to send some questionnaires out to you to complete again when your child is nine years old. If you decide to take part we will write to your GP and your child's GP to inform them you have agreed to do so.

**What will we have to do?**
**At age 7 years**

- One of our specially trained research assistants would like to see you and your first child at home together for 1-2 hours.
- We will ask you to complete an interview and questionnaires about your personal circumstances, your lifestyle, recent accidents and events, relationships, your personality, emotional wellbeing and your physical health. We will ask about your first child's health, behaviours, physical and emotional development and about the parenting decisions you make on a day to day basis.
- We would like to ask you and your child to play together for a short time and then talk together about rules that affect children. We would also like you to plan an activity together. We will make a short DVD of the conversation between the two of you. We will be looking at your child's behaviours during this play time together and the different parenting skills you use.
- We will show your child some photographs of faces on a computer screen and ask him/her to say or show us which emotion is being shown.
- We will show your child some pictures that have been previously used in child research and chosen to be suitable for children aged 7-11 years of age. We will ask them to tell us how they feel whilst looking at them. We will then play them some sounds and ask them how they felt whilst listening to them.
- We would like to find out about your child's mental development by giving him/her some puzzles, games and memory tasks to complete.
- We will assess your child's vocabulary and understanding of words.
- We would also like to collect saliva from your child to assess DNA and gene activity. Each child will be asked to spit into a small collection pot, so we can collect enough saliva for analysis at age 7 years.
- We will weigh your child and measure their height, upper arm and head size.
- We would also like to ask you for permission to contact your child's teacher to ask if he / she can complete some questionnaires about your child's behaviours, emotions, relationship with peers and progress in school at age 7. We will send a copy of your consent to do this to the school nurse for their records.

**At age 9 years**

- We will also send you a booklet of questionnaires to complete when your child is nine years old. This will take about 45 minutes to complete. We will provide a freepost envelope for you to send it back to us.
- We would also like to ask you for permission to contact your child's teacher to ask if he / she can complete some questionnaires about your child's behaviours, emotions, relationship with peers and progress in school at age 9. We will send a copy of your consent to do this to the school nurse for their records.
- We wish to follow the families in the study for a long time as their children grow up and so if we get funding to do this we may ask you later to consider being in the study for longer.

For now, we are asking you to take part in this study over a three year period from when your child is 7 years old until they are 9 years old.

**Expenses and payments**
We are able to give you £30 in high street shopping vouchers at age 7 for the home visit and £20 for the questionnaire at age 9 years. This is to compensate you for time lost from home or work and any other expenses incurred from taking part in the study.

**Will my taking part in the study be kept confidential?**

- Information on DVD recordings, on audio recordings of interviews with you, and on paper questionnaire records and any information we enter on computers about you will be identified only by a case number. A computer database and paper copies of participant names and addresses and contact details and their case numbers will be kept separately and securely in the university study base so no-one outside of the research team can access this or identify you or your child. All the information you give us is therefore 'pseudo-anonymised' which means that it is identified ONLY by a case number and ONLY the research team will be able to link your case number to who you are and the other contact information you give us.
- We would like to make DVD recordings of your child and you so that we go over what happened in detail afterwards. The recordings will be identified only by a case number, so that information on it cannot be traced to you by anyone outside of the research team. A copy of the recording will be kept securely at each university base for up to thirty years.
- The genetic samples will be analysed pseudo-anonymously too. This means that no records will be generated that directly link your name, your partner's name, or your child's name to the genetic samples. Instead, they will be linked only by the case number. So only the research team will know who the samples belong to. We will analyse the samples for genes that affect childrens' health, emotions and behaviour, and not for any other purpose. They will not be kept as part of your medical record. All samples will be destroyed after 20 years. The pseudo-anonymous samples will be analysed by a laboratory technician who will have no access to your name, your partner's name, or your child's name.
- All information that we receive from you will be treated as strictly confidential, under the guidelines of the Universities of Liverpool and Reading, the UK Medical Research Council, and the Data Protection Act. This means that your information will only used by members of the research team and scientific research collaborators from other academic institutions approved by us.
- We will report general research findings about parents and children, and you or your child will never be identified. Reports will be based on the ratings that we make from the interviews, observations, questionnaires or DVD recordings and on occasions when examples of individual responses are reported these will be fully pseudo-anonymised.
- The only reason we might have to share information from the study with other people is if there are concerns about you or a child being at risk of serious harm. If that happens we will talk with you first to decide on the best way forward. Concerns like this would be addressed by seeking appropriate forms of help for you and by following Trust Child Protection Guidelines.

**What will happen to the results of the research study?**
We will publish the results of this study in academic journals, at international and national conferences and we will inform study participants of key findings in a study newsletter sent to your home. We also plan to develop a study website where results will be displayed.

**What will happen when the research study stops?**
When this part of the research comes to an end we hope to secure further funding to continue studying all the families and the children as they grow up through the school years. We would of course ask your permission to do this at a later date.

**What are the possible benefits to taking part?**
There are no benefits to you or your child's health in taking part in this study. However we hope that you will feel you are contributing to medical research in a way that will help children and families in the future.

**What are the possible disadvantages and risks to myself or my child taking part in this study?**
No, there are no known or likely risks. It is possible that your child may become a little upset when viewing emotional pictures. If this occurs the researcher will ask you if you wish to take a break or continue. You may also choose to stop their assessments completely at any time. Of course, your child is also free to say no to any task or procedure.

**Who is organising and funding the research?**
The study is being led jointly by Professor Jonathan Hill of the University of Reading and Dr Helen Sharp of the University of Liverpool. The research is funded by the Medical Research Council.

**Who has reviewed and approved the study?**
A team of international experts on child development has reviewed this study for the Medical Research Council. The study has been reviewed and approved by the Research & Development committees of Wirral Community NHS Trust and Cheshire and Wirral Partnership NHS Foundation Trust, the National Ethics Research Service Northwest – Haydock, and The University of Reading Research Ethics Committee.

**What if there is a problem?**
*Complaints*
If you have a concern about any aspect of this study, you should ask to speak to Professor Hill and Dr Helen Sharp or a member of their research team who will do their best to answer your questions. If they are unable to resolve your concern or you wish to make a complaint regarding the study, please contact the Head of the School of Psychology and Clinical Language Sciences, Professor Laurie Butler on 0118 378 5743 or by email to l.t.butler@reading.ac.uk

*Harm*
In the event that something does go wrong and you or your child are harmed during the research you may have grounds for a legal action for compensation against The University of Reading and The University of Liverpool but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

**Further information and contact details:**
When the researcher meets you they will be very happy to answer any questions you might have. In the meantime, if you would like any more information, please do not hesitate to contact Professor Jonathan Hill, Dr Helen Sharp or Liz Green / Karen Rafferty (study administrators) on the freephone number shown on the front page.

**Appendix 2 (continued) - Participant information sheets, phase 6.**



MANCHESTER 1824

Wirral University Teaching Hospital NHS
NHS Foundation Trust

The University of Manchester

UNIVERSITY OF LIVERPOOL


**Study Base:**
**The Lauries Centre, 142 Claughton Road,**
**Birkenhead, Wirral, CH41 6EY**
**Freephone: 0800 051 7597**
**(from a mobile) 800 051 7597**
**Text: 07956 297412**

**Parent Information Sheet – Study 300**

**Title of study : The Wirral Child Health and Development Study**

**Investigators: Jonathan Hill, Helen Sharp, Andrew Pickles, Gill Lancaster**
**Research Staff: Karen Lunt, Carol Bedwell, Belinda Thompson, Julie Carlisle, Kate Marks, Nichaela Broyden, Kate Marshall, Florin Tibu, Carol Sadler, Jo Roberts, Jenny Lee, Liz Green**

When you were pregnant, and again just after your baby was born you kindly helped us with a study that we are conducting designed to understand better how stress affects mothers to be, their partners and their babies, and how good experiences and support can make a difference. We are following 1500 women up to the first birthday of their babies mainly using questionnaires. In addition we are asking 300 to take part in interviews and to agree to us filming their babies during the first year of their life. You are one of the 300 that we would like to see again now that your baby is nearly 6 months old. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part. Thank you for reading this.

**What is the study about?**
The aim of the study is to find out about the effects of stress on parents and children during the antenatal period and in the first months after birth. We plan to measure each baby's development and how they interact with their mother in some detail. We believe that for some parents and children the effects are quite long lasting, and others find ways of coping. We want to understand these processes better so that services to support families experiencing stress can be improved. We are focussing on mothers for this detailed part of the study because most babies spend most time with their mother.

**Who is being invited to take part?**
The computer chooses the names of women who we approach based on the information they have given about how much stress they may be experiencing. Because we particularly want to understand about stress in pregnancy the computer is picking more women who are experiencing stress. Your name has been chosen either because you have indicated that you are dealing with quite a lot of stress or because you have said you are not facing a lot.

**Do I have to take part?**
It will be up to you to decide whether or not you would like to take part. If you agree, and change your mind later, you can withdraw from the study. This will not affect the care you receive.

**How often will I be contacted?**
Now that your baby is nearly 6 months old we would like to visit you and your baby at home and to come to our study centre for about 1½ hours, We will ask to see you again close to your baby's first birthday.

**What will we have to do?**

- We would like to see you and your baby once at home and once at the Study Centre. You will be with your baby at all times.
- We will talk with you about your feelings and experiences since the last visit, and ask you about your baby's usual behaviour. We will audio tape part of this talk.
- We would like to make a short video (about 20 minutes) of your baby playing with you .
- We will also make a video of how your baby responds to everyday events such as watching new things, the researcher talking and playing with them, hearing a loud noise or not being allowed to play with a toy for a short time.
- We will put three patches on your baby's back or chest to record your baby's heart while we are watching your baby.
- We will gather two saliva samples from your baby by wiping a cotton swab in his/her mouth at the start of the visit to the Study Centre and once again at the end. This is completely safe and will be used to measure your baby's stress hormones.

**Will my expenses be paid?**
We will be pleased to organise transport to the interview, or to pay for your transport. We are able to pay up to £30 to compensate you for time lost from home or work or any other expenses incurred from taking part in the study.

**How will this information be used?**

- We would like to make a video recording of your baby and you so that we go over what has happened in detail afterwards. The recording will be identified only by a number, so that information on it cannot be traced to you. The recording will be kept secure at the university base for up to ten years.
- All information that we receive from you will be treated as strictly confidential, under the guidelines of the Universities of Liverpool and Manchester, the UK Medical Research Council, and the Data Protection Act.
- Information on audio and video recordings, on paper records, and that we enter on to the computer will be identified only by a number. A list of names and addresses of participants and their case numbers will be kept separately and securely in the university base.
- We will report general findings about parents and children, and you or your child will never be identified. Reports will only be based on the ratings that we make from the interview and none of what you say will be reported.
- The only reason we might have to share information from the study with other people is if there are concerns about you or a child being at risk of serious harm. If that happens we will talk with you first to decide on the best way forward. Concerns like this would be addressed by seeking appropriate forms of help for you and following Trust Child Protection Guidelines.

**Who is organising and funding the research study?**
The study is being run by Professor Jonathan Hill of the University of Manchester and Dr Helen Sharp of the University of Liverpool. The research is funded by the Medical Research Council.

**Are there any benefits in taking part in this study?**
There are no benefits to your or your child's health in taking part in this study. However we hope that you will feel you are contributing to medical research in a way that will help children and families in the future.

**What if something goes wrong?**
If you feel you or your child have been harmed by taking part in this research and that the researchers have been negligent or at fault, then you may be able to make a legal claim for compensation to their employer. You might have to pay the legal costs of doing this. However, if you are harmed and the researchers are not at fault, there is no facility for you to make a claim. If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during the course of this study, normal University or National Health Service complaints procedures should be available to you.

**Are there any risks to myself or my child taking part in this study?**
No, there are no known or likely risks.

**Who has reviewed and approved the study?**
A team of international experts on child development has reviewed this study for the Medical Research Council. The study has been reviewed and approved by the Research & Development committees of Wirral Hospitals NHS Trust, Wirral Primary Care Trust and the Cheshire Local Research Ethics Committee.

**Can I ask further questions?**
When the researcher meets you they will be very happy to answer any questions you might have. In the meantime, if you would like any more information, please do not hesitate to contact Professor Jonathan Hill, Dr Helen Sharp, or Liz Green on the freephone number shown on the front page.

## Appendix 2 (continued) – Participant information sheet phase 8



MANCHESTER 1824

The University of Manchester

Wirral University Teaching Hospital NHS
NHS Foundation Trust

UNIVERSITY OF LIVERPOOL


Study Base:
The Lauries Centre, 142 Claughton Road,
Birkenhead, Wirral, CH41 6EY
Freephone: 0800 051 7597
(from a mobile) 800 051 7597
Text: 07956 297412

**Parent Information Sheet – Study 300**

**Title of study : The Wirral Child Health and Development Study**

**Investigators: Jonathan Hill, Helen Sharp, Andrew Pickles, Gill Lancaster**
**Research Staff: Kate Marks, Florin Tibu, Kate Marshall, Melissa Bensinyor, Helen Jones, Liz Green, Nicola Sandman, Alice Hulbert, Kirsty Entwistle, Gemma Culverwell, Louise Fisher, Stuart Kehl, Fay Huntley**

When you were pregnant, and again just after your baby was born you kindly helped us with a study that we are conducting designed to understand better how stress affects mothers to be, their partners and their babies, and how good experiences and support can make a difference. We are following 1500 women up to the first birthday of their babies mainly using questionnaires. In addition we are asking 300 to take part in interviews and to agree to us filming their babies during the first year of their life. You are one of the 300 that we would like to see again now that your baby is one year old. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part. Thank you for reading this.

**What is the study about?**
The aim of the study is to find out about the effects of stress on parents and children during the antenatal period and in the first months after birth. We plan to measure each baby's development and how they interact with their mother in some detail. We believe that for some parents and children the effects are quite long lasting, and others find ways of coping. We want to understand these processes better so that services to support families experiencing stress can be improved.

Our research team is very interested to know more about the genes that influence children's emotions and behaviours. Every child is a unique individual, and that is partly due to the genes that have been passed on from each parent. Genes are like maps inside our bodies that hold information. For example, it is well known that the colour of our eyes depends on our genes. More recently we have learnt much more about how health and behaviour are influenced by genes. This study provides an important opportunity to learn more about the ways in which genes affect the way infants behave and their ability to cope with new situations.

**Who is being invited to take part?**
The computer chooses the names of women who we approach based on the information they have given about how much stress they may be facing. Because we particularly want to understand about stress in pregnancy the computer is picking more women who are experiencing stress. Your name has been chosen either because you have indicated that you may be dealing with quite a lot of stress or because you have said you are not facing a lot.

**Do I have to take part?**
It will be up to you to decide whether or not you would like to take part. If you agree, and change your mind later, you can withdraw from the study. This will not affect the care you receive.

**How often will I be contacted?**
Now that your baby is one year old we would like you and the baby to come to our study centre for about half a day. We are planning further contacts for the future and we hope we will be able to obtain funding to see you again when your baby is around two to two and a half years old.

**What will we have to do?**

- We would like to see you and your child at the Lauries Centre for half a day.
- We will talk with you about your feelings and experiences since the last visit and audio record our conversation.
- We will ask you about your child's behaviours and emotions. For example we will ask what makes him/her anxious, or angry, or happy, and what he/she likes to do with you. We will audio record this conversation also.
- We would like to make a short video (about 15 minutes) of your baby playing with you with some toys .
- We would like to make a video of how your baby responds to everyday events such as playing with various toys, seeing an unusual character or not being allowed to play with a toy for a short time.
- We would also like to make a video of how your child responds to being separated from you. Some children find this quite hard and others are not worried by it. You will be able to see your child's response and if he or she is distressed by it you will be able to comfort him/her straight away. This experience is designed to mimic or copy natural times at home when you have to separate for a short time, for example while you go briefly into another room.
- We will put two patches on your baby's chest (just as we did when your baby was younger) to record your baby's heart during video recordings of your baby and of the separation and when he/she is with you again.
- We are also going to see whether some babies are more likely to produce the kinds of hormones that help them to deal with challenging situations. To do this, all we have to do is ask your baby to chew on a soft, cotton dental roll, which is completely safe, and will not produce any allergic reactions. This allows us to collect a sample of your baby's saliva, which can then be analysed to measure the hormones. We would like to do this four times, once before, and once after the separation from you, and once before and once after a toy play task
- We would also like to collect saliva from your baby for DNA analysis using a similar cotton swab.
- We would like to find out about your child's development by giving him/her some puzzles to solve.
- We will weigh your child and measure their height and head size.

**Will my expenses be paid?**
We will be pleased to organise transport to the interview, or to pay for your transport. We are able to pay up to £30 to compensate you for time lost from home or work or any other expenses incurred from taking part in the study.

**How will this information be used?**

- We would like to make a video recording of your baby and you so that we go over what has happened in detail afterwards. The recording will be identified only by a number, so that information on it cannot be traced to you. The recording will be kept secure at the university base for up to ten years.
- All information that we receive from you will be treated as strictly confidential, under the guidelines of the Universities of Liverpool and Manchester, the UK Medical Research Council, and the Data Protection Act.
- Information on audio and video recordings, and on paper records, and that we enter on to the computer will be identified only by a number. A list of names and addresses of participants and their case numbers will be kept separately and securely in the university base.
- The genetic samples will be analysed anonymously. No records will be generated that directly link your name, your partner's name, or your child's name to the genetic samples. They will only be analysed for the purpose of this study, and will never be analysed for any other purpose. We will analyse the samples for genes that affect infants' emotions and behaviour, and not for any other purpose. They will not be kept as part of your medical record. All samples will be destroyed after 20 years. The anonymous samples will be analysed by a laboratory technician who is not affiliated with the study, and will have no access to your name, your partner's name, or your child's name.
- We will report general findings about parents and children, and you or your child will never be identified. Reports will only be based on the ratings that we make from the interview and none of what you say will be reported.
- The only reason we might have to share information from the study with other people is if there are concerns about you or a child being at risk of serious harm. If that happens we will talk with you first to decide on the best way forward. Concerns like this would be addressed by seeking appropriate forms of help for you and following Trust Child Protection Guidelines.

**Who is organising and funding the research study?**
The study is being run by Professor Jonathan Hill of the University of Manchester and Dr Helen Sharp of the University of Liverpool. The research is funded by the Medical Research Council.

**Are there any benefits in taking part in this study?**
There are no benefits to your or your child's health in taking part in this study. However we hope that you will feel you are contributing to medical research in a way that will help children and families in the future.

**What if something goes wrong?**
If you feel you or your child have been harmed by taking part in this research and that the researchers have been negligent or at fault, then you may be able to make a legal claim for compensation to their employer. You might have to pay the legal costs of doing this. However, if you are harmed and the researchers are not at fault, there is no facility for you to make a claim. If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during the course of this study, normal University or National Health Service complaints procedures should be available to you.

**Are there any risks to myself or my child taking part in this study?**
No, there are no known or likely risks.

**Who has reviewed and approved the study?**
A team of international experts on child development has reviewed this study for the Medical Research Council. The study has been reviewed and approved by the Research & Development committees of Wirral University Teaching Hospital NHS Trust, Wirral Primary Care Trust, Western Cheshire PCT and the Cheshire Local Research Ethics Committee.

**Can I ask further questions?**
When the researcher meets you they will be very happy to answer any questions you might have. In the meantime, if you would like any more information, please do not hesitate to contact Professor Jonathan Hill, Dr Helen Sharp or Liz Green on the freephone number shown on the front page.

## Appendix 2 (continued)- Participant information sheets, phase 9, 10 and 11



The University of Manchester


Study Base:
The Lauries Centre,
142 Claughton Road
Birkenhead, Wirral,
CH41 6EY
Freephone: 0800 051 7597
(from a mobile) 800 051 7597
Text: 07956 297412

### Participant Information Sheet

**Title of study : The Wirral Child Health and Development Study 1-4 years**

**Investigators: Jonathan Hill, Helen Sharp, Andrew Pickles, John Quinn, Vivette Glover. Research Staff: Liz Green, Niki Sandman, Kate Marshall, Helen Jones, Louise Fisher, Stuart Kehl, Fay Huntley, Nicky Wright.**

When you were pregnant, just after your baby was born and when your baby was 12 months old you kindly helped us with this research study. We are now inviting you to take part in this study until your first child is just over 4 years old.

Before you decide whether you want to take part in the next stages of the study, it is important for you to understand why the research is continuing and what it will involve for you and your child. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part. Thank you for reading this.

**What is the purpose of the study?**
This study aims to find out how children learn how to behave with other people, and why some children have difficulties controlling their behaviours. To do this we need to measure many aspects of their early development, their experiences, and the ways parents take care of them. We are interested to find out more about the ways that early life stress influences later development as we know that for some parents and children the effects are quite long lasting, and others find ways of coping. Every child is a unique individual and that is partly due to the genes that have been passed on from each parent and partly due to individual life experiences. Genes are like maps inside our bodies that hold information. We now also know that health and behaviour are influenced by genes. This information in our genes is stored in 'DNA', which can be found in our skin cells and saliva. We now also know that genes only influence development when they are switched on. We can tell whether genes are switched on or off at a particular time point from something called 'RNA' which can also be found in our skin cells or saliva. In this study we want to find out more about how genes and different life experiences influence parent's and children's behaviours and development so that NHS services that support families can be improved with this knowledge.

**Why have I been invited to take part?**
At the time when you were expecting your first child, we approached all women who were booked into the antenatal clinic at Arrowe Park Hospital for their antenatal care over a two year period. During this time we recruited 1286 mothers who were experiencing low, medium or high levels of stress in pregnancy. We asked all mothers reporting higher levels of stress and a sub-group of mothers chosen by the computer at random who were reporting lower levels of stress, to take part in an 'intensive' part of the study. You were one of these mothers and we would like now to follow your child's development up to four years of age if you are happy for us to do so.

NHS Western Cheshire

NHS Wirral

**Do I have to take part?**
It will be up to you to decide whether or not you would like to take part. If you agree, and change your mind later, you can withdraw from the study. This will not affect the care you receive. If you choose to take part and you find you do not wish to complete a particular assessment or answer a particular question, you will be free to miss that part out but carry on with the rest of the study if you wish or you can just choose to stop that assessment completely.

**What will happen to me if I take part ?**
We would like to meet with you and your baby when he or she is two, three and four years of age to complete a range of adult interviews, mother-child assessments in the study base, questionnaire packs and a home visit. If you decide to take part we will write to your GP and your child's health visitor to inform them you have agreed to do so.

**What will we have to do?**

**When your child is 2 and 3 years old**

***Adult interview***

- We will talk in detail with you about your feelings, relationships, supports and life experiences since the last visit and audio record our conversation. These interviews will be similar to the ones you have completed on previous occasions.
- Now your child is a toddler we will ask in detail about their development and health including illnesses, accidents, injuries and treatments received since birth. We will ask about your parenting practices including childcare arrangements and daily activities with your child.
- This interview will be done at The Lauries or at home, whichever you prefer.

***Mother and child visit to The Lauries***

- We would like to see you and your child at the Lauries Centre for half a day.
- We will ask you about your child's behaviours and emotions. For example we will ask what makes him/her anxious, or angry, or happy, and what he/she likes to do with you. We will audio record this conversation also.
- We would like to make a short video (about 15 minutes) of your infant playing with you with some toys and tidying them away at the end. We will be looking at your infant's behaviours during this play time together and the different parenting skills you use.
- We would like to make a DVD of how your baby responds to everyday events such as playing with various toys, exploring a new room with several odd-looking toys or not being allowed to play with a toy for a short time. You will be given a copy of the DVD to keep.
- We would like to find out about your child's development by giving him/her some puzzles to solve.
- We will put three patches on your infant's back (just as we did when your infant was younger) to record your baby's heart during these games and puzzles and a conversation with you. We will make a DVD recording of this too.
- We are also going to see whether some infants are more likely to produce the kinds of hormones that help them to deal with challenging situations. To do this, we will collect some of his/her saliva wiping a set of very small soft sponges in their mouth for 90 seconds at a time. We will blow bubbles while this is done to keep them happy. These soft sponges are smaller than the cotton dental roll we used last time when your baby was one year old. This is a new safe system for infants, and will not produce any allergic reactions. Once we have collected a sample of your infant's saliva it can then be analysed to measure the hormones. We would like to do this four times, once before, and once after exploring the new room with odd looking toys in it, and once before and once after a conversation task with you.
- We would also like to collect skin cells with saliva from your baby's mouth to assess gene activity (RNA analysis) at each time point by briefly rubbing small cotton buds on the inside of your infants cheeks.
- We wish to collect a sample of your own skin cells with saliva from the inside of your mouth for DNA analysis by briefly rubbing small cotton buds on the inside of your cheeks. This is so we can investigate possible links between maternal genes and parenting behaviours.
- We will weigh your child and measure their height, upper arm and head size.

**At 3 years only**

- We will show your child some photographs of faces (like we did with you when you were pregnant) and ask him/her to say which emotion it is.
- We would also like to visit you about an hour both to see how your child learns and gets along with you at home.

**At 4 years only**

- We will talk in detail with you about your feelings, relationships, supports and life experiences since the last visit and audio record our conversation. These interviews will be similar to the ones you have completed on previous occasions.
- Now your child will soon start school we will ask in detail about their development and health including illnesses, accidents, injuries and treatments received over the past year. We will ask about your parenting practices including childcare arrangements and daily activities with your child.
- We will ask you in detail about your child's emotions and behaviours

We wish to follow the families in the study for a long time as their children grow up and so if we get funding to do this we may ask you later to consider being in the study for longer. But for now, we are asking you to take part in this study over a three year period from when your child is about 2 years old until they are about 4 ½ years old. Now your child is a toddler we are hoping to study parenting and child behaviours in greater detail than was possible in the earlier stages of your baby's life. At each stage of the study, specially trained research assistants will complete the study interviews or assessments with you and your baby.

**Expenses and payments**

We are able to give you £40 in high street shopping vouchers each time you complete a yearly assessment. This is to compensate you for time lost from home or work and any other expenses incurred from taking part in the study.

**Will my taking part in the study be kept confidential?**

- Information on DVD recordings, on audio recordings of interviews with you, and on paper questionnaire records and any information we enter on computers about you will be identified only by a case number. A computer database and paper copies of participant names and addresses and contact details and their case numbers will be kept separately and securely in the university study base so no-one outside of the research team can access this or identify you or your child. All the information you give us is therefore 'pseudoanonymised' which means that it is identified ONLY by a case number and ONLY the research team will be able to link your case number to who you are and the other contact information you give us.
- We would like to make DVD recordings of your baby and you so that we go over what happened in detail afterwards. The recordings will be identified only by a case number, so that information on it cannot be traced to you by anyone outside of the research team. A copy of the recording will be kept securely at each university base for up to thirty years.
- The genetic samples will be analysed pseudo-anonymously too. This means that no records will be generated that directly link your name, your partner's name, or your child's name to the genetic samples. Instead, they will be linked only by the case number. So only the research team will know who the samples belong to. We will analyse the samples for genes that affect infants' health, emotions and behaviour, and not for any other purpose. They will not be kept as part of your medical record. All samples will be destroyed after 20 years. The pseudo-anonymous samples will be analysed by a laboratory technician who is not affiliated with the study, and will have no access to your name, your partner's name, or your child's name.
- All information that we receive from you will be treated as strictly confidential, under the guidelines of the Universities of Liverpool and Manchester, the UK Medical Research Council, and the Data Protection Act. This means that your information will only used by members of the research team and scientific research collaborators from other academic institutions approved by us.
- We will report general research findings about parents and children, and you or your child will never be identified. Reports will be based on the ratings that we make from the interviews, questionnaires or DVD recordings and on occasions when examples of individual responses are reported these will be pseudo-anonymised.
- The only reason we might have to share information from the study with other people is if there are concerns about you or a child being at risk of serious harm. If that happens we will talk with you first to decide on the best way forward. Concerns like this would be addressed by seeking appropriate forms of help for you and by following Trust Child Protection Guidelines.

**Appendix 2 (continued) – Participant information sheet phase 13 intensive**


Study Base:
The Laurie: Centre,
142 Claughton Road
Birkenhead, Wirral,
CH41 6EY
Freephone: 0800 051 7597
(from a mobile) 800 051 7597
Text: 07956 297412

## Participant Information Sheet

**Title of study: The Wirral Child Health and Development Study 7-9 years**

**Investigators: Jonathan Hill, Helen Sharp, Andrew Pickles, John Quinn, Chris Murgatroyd.**
**Research Staff: Kay Martin, Karen Rafferty, Kate Abbott, Helen Chadwick, Louise Fisher, Stuart Kehl, Nicky Wright, Matthew Bluett-Duncan and Miriam Refberg**

When you were pregnant and during the first five years of your first child's life you have kindly helped us with this research study. We would very much like to thank you for helping us for all this time and we would like now to invite you to take part until he or she is 9 years old.

Before you decide whether you want to take part in the next stages of the study, it is important for you to understand what it will involve for you and your child. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part. Thank you for reading this.

**What is the purpose of the study?**
This study aims to find out how children learn how to behave with other people as they grow up, and why some children have difficulties controlling their behaviours. To do this we need to measure many aspects of their development, their experiences at home and school, and the ways parents take care of them. We are interested to find out more about the ways that early life stress influences later development as we know that for some parents and children the effects are quite long lasting, and others find ways of coping. We know also that as children reach the school years they learn more complex ways of making sense of the world around them, so we plan to study how children understand emotions, how they think about and respond individually to social challenges. Every child is a unique individual and that is partly due to the genes that have been passed on from each parent and partly due to individual life experiences. Genes are like maps inside our bodies that hold information. We also know that health and behaviour are influenced by genes. This information in our genes is stored in 'DNA', which can be found in our saliva. We also now know that genes only influence development when they are switched on. We can tell whether genes are switched on or off at a particular time point from looking closely at the DNA and from something called 'RNA' which can also be found in our saliva. In this study we plan to collect more saliva for DNA analysis at age 7 so we can continue to monitor the activity levels of genes thought to influence behaviour and emotional responses, as children gain new life experiences. We want to find out more about how genes and different life experiences influence parent's and children's behaviours and development so that NHS and educational services that support families can be improved with this knowledge.

**Why have I been invited to take part?**
At the time when you were expecting your first child, we approached all women who were booked into the antenatal clinic at Arrowe Park Hospital for their antenatal care over a two year period. During this time we recruited 1286 mothers who were experiencing low, medium or high levels of stress in pregnancy. We asked all mothers reporting higher levels of stress and a sub-group of mothers chosen by the computer at random who were

reporting lower levels of stress, to take part in an 'intensive' part of the study. You were one of these mothers and we would like now to follow your child's development up to nine years of age if you are happy for us to do so.

**Do I have to take part?**
It will be up to you to decide whether or not you would like to take part. If you agree, and change your mind later, you can withdraw from the study. This will not affect the care you receive. If you choose to take part and you find you do not wish to complete a particular assessment or answer a particular question, you will be free to miss that part out but carry on with the rest of the study if you wish or you can just choose to stop that assessment completely.

**What will happen to me if I take part?**
We would like to meet with you and your child when he or she is 7 years and 9 years of age to complete a range of adult interviews, mother-child assessments in the study base, and questionnaire packs. If you decide to take part we will write to your GP and your child's GP to inform them you have agreed to do so.

**What will we have to do?**

**When your child is 7 years old**

*Adult interview*

- We will talk in detail with you about your health, feelings, relationships, supports and life experiences since the last visit and audio record our conversation. These interviews will be similar to the ones you have completed on previous occasions.
- We will ask in detail about your child's development and health including illnesses, sources of previous harm and accidents, injuries and treatments received since the last time we met you. We will ask about your parenting practices including childcare arrangements, your thoughts about child behaviours and how you respond to them.
- This interview will be done at The Lauries or at home, whichever you prefer.

*Mother and child visit to The Lauries*

- We would like to see you and your child at the Lauries Centre for half a day. This may be split into two shorter visits to suit you and your child.
- We would like to ask you and your child to play together for a short time and then talk together about rules that affect children and about different emotional times, such as when your child was scared, naughty, or sad, and a time when you had to keep them safe. We will video record the conversation between the two of you.
- We will ask you to draw a picture together, eat a snack together, plan an activity together, followed by a short time when you will be asked to show your child affection as you might do at home. We will be video recording your child's behaviours during this play-time together and the different parenting skills you use.
- We will show your child some photographs of faces on a computer screen and ask him/her to say or show us which emotion is being shown. Sometimes he/she will need to match the face to one that shows the same emotion and other times he/she will be asked to pick out the name of the emotion. During this task the computer will track your child's eye-gaze so we can see which parts of the faces they look at.
- We will show your child some pictures that have been previously used in child research and chosen to be suitable for children aged 7-11 years of age. We will ask them to tell us how they feel whilst looking at them. We will then play them some sounds and ask them how they felt whilst listening to them.
- We will show your child a short 8 minute emotional film taken from an old ITV children's program, followed by short clips from that video and we will ask how each one makes your child feel. There will be parts in which the boy character is scared, angry, sad and happy.
- We would like to find out about your child's mental development by giving him/her some puzzles, games and memory tasks to complete.
- We will assess your child's vocabulary and understanding of words.
- We will ask your child to play the Cyber-ball game which is a computerised ball throwing game. During this game your child will experience being included in the game for a short period and half the children, picked at random by the computer, will also then experience a short period of not being included in the

ball throwing game. Children in their everyday lives commonly experience short periods of inclusion and exclusion during play. We will then measure how your child responds to video clips about other children's behaviour immediately following the ball game. Finally all children will end with a period of being included in the ball throwing game again.

- We would like to measure your child's physiological response to all the emotional tasks by measuring his/her skin response. We will put two sticky pads on his/her two fingers during some of the development assessments to do this.
- We would also like to put three patches on your child's back to record their heart rate during the time in the child development unit.
- We will also try to see whether some children are more likely to produce the kinds of hormones that help them to deal with challenging situations. To do this, we will collect some of his/her saliva by wiping a set of very small soft sponges in their mouth for 90 seconds at a time. This is a safe system for children, and will not produce any allergic reactions. Once we have collected a sample of your child's saliva it can then be analysed to measure the hormones. We would like to do this three times, once when you arrive in the unit, once later after some games and puzzles and once after viewing the emotional film.
- We would also like to collect saliva from your child to assess DNA and gene activity. Each child will be asked to spit into a collection pot, like that used at age 4-5 years of age, so we can collect enough saliva for analysis at age 7 years.
- We will weigh your child and measure their height, upper arm and head size.
- We will ask you to complete a number of questionnaires, like at previous phases of the study, about changes in your home circumstances, health and lifestyle, school, family life and yours and your child's physical and mental health and behaviours.
- We would also like to ask you for permission to contact your child's teacher to ask if he / she can complete some questionnaires about your child's behaviours, emotions, relationship with peers and progress in school. We will send a copy of your consent to do this to the school nurse for their records.
- We will make a DVD recording of the whole session for the study and you will be given a copy to keep.

**At 9 years only**

- We will talk in detail with you about your health, feelings, relationships, supports and life experiences since the last visit and audio record our conversation. These interviews will be similar to the ones you have completed on previous occasions.
- We will ask in detail about your child's development and health including illnesses, sources of previous harm and accidents, injuries and treatments received since the last time we met you. We will ask about your parenting practices including childcare arrangements, your thoughts about child behaviours and how you respond to them.
- We will ask you to complete a number of questionnaires, like at previous phases of the study, about changes in your home circumstances, health and lifestyle, school, family life and yours and your child's physical and mental health and behaviours.
- We would also like to ask you for permission to contact your child's teacher to ask if he / she can complete some questionnaires about your child's behaviours, emotions, relationship with peers and progress in school at age 9.
- This interview will be done at The Lauries or at home, whichever you prefer.

We wish to follow the families in the study for a long time as their children grow up and so if we get funding to do this we may ask you later to consider being in the study for longer. But for now, we are asking you to take part in this study over a three year period from when your child is about 7 years old until they are 9 years old. Now your child is in school we are hoping to study child behaviours in greater detail, across home and school, wherever possible. At each stage of the study, specially trained research assistants will complete the study interviews or assessments with you and your child.

**Expenses and payments**

We are able to give you £50 in high street shopping vouchers each time you complete a yearly assessment. This is to compensate you for time lost from home or work and any other expenses incurred from taking part in the study.

**Will my taking part in the study be kept confidential?**

- Information on DVD recordings, on audio recordings of interviews with you, and on paper questionnaire records and any information we enter on computers about you will be identified only by a case number. A computer database and paper copies of participant names and addresses and contact details and their case numbers will be kept separately and securely in the university study base so no-one outside of the research team can access this or identify you or your child. All the information you give us is therefore 'pseudo-anonymised' which means that it is identified ONLY by a case number and ONLY the research team will be able to link your case number to who you are and the other contact information you give us.
- We would like to make DVD recordings of your child and you so that we go over what happened in detail afterwards. The recordings will be identified only by a case_number, so that information on it cannot be traced to you by anyone outside of the research team. A copy of the recording will be kept securely at each university base for up to thirty years.
- The genetic samples will be analysed pseudo-anonymously too. This means that no records will be generated that directly link your name, your partner's name, or your child's name to the genetic samples. Instead, they will be linked only by the case_number. So only the research team will know who the samples belong to. We will analyse the samples for genes that affect children's health, emotions or behaviour, and not for any other purpose. They will not be kept as part of your medical record. All samples will be destroyed after 20 years. The pseudo-anonymous samples will be analysed by a laboratory technician who will have no access to your name, your partner's name, or your child's name.
- All information that we receive from you will be treated as strictly confidential, under the guidelines of the Universities of Liverpool and Reading, the UK Medical Research Council, and the Data Protection Act. This means that your information will only used by members of the research team and scientific research collaborators from other academic institutions approved by us.
- We will report general research findings about parents and children, and you or your child will never be identified. Reports will be based on the ratings that we make from the interviews, laboratory tasks, questionnaires or DVD recordings and on occasions when examples of individual responses are reported these will be pseudo-anonymised.
- The only reason we might have to share information from the study with other people is if there are concerns about you or a child being at risk of serious harm. If that happens we will talk with you first to decide on the best way forward. Concerns like this would be addressed by seeking appropriate forms of help for you and by following Trust Child Protection Guidelines.

**What will happen to the results of the research study?**

We will publish the results of this study in academic journals, at international and national conferences and we will inform study participants of key findings in a study newsletter sent to your home. We also plan to develop a study website where results will be displayed.

**What will happen when the research study stops?**

When this part of the research comes to an end we hope to secure further funding to continue studying all the families and the children as they grow up through the school years. We would of course ask your permission to do this at a later date.

**What are the possible benefits to taking part?**

There are no benefits to you or your child's health in taking part in this study. However we hope that you will feel you are contributing to medical research in a way that will help children and families in the future.

**What are the possible disadvantages and risks to myself or my child taking part in this study?**

No, there are no known or likely risks. It is possible that you may become upset when recalling difficult experiences in your life. If this occurs the interviewer will ask you if you wish to take a break from interviewing or continue. You may also choose to stop the interview completely at any time. It is possible that your child may become a little upset when viewing emotional pictures or videos. If this occurs the researcher will ask you if you wish to take a break or continue. You may also choose to stop their assessments completely at any time. Of course, your child is also free to say no to any task or procedure.

**Who is organising and funding the research?**
The study is being led jointly by Professor Jonathan Hill of the University of Reading and Dr Helen Sharp of the University of Liverpool. The research is funded by the Medical Research Council.

**Who has reviewed and approved the study?**
A team of international experts on child development has reviewed this study for the Medical Research Council. The study has been reviewed and approved by the Research & Development committees of Wirral Community NHS Trust and Cheshire and Wirral Partnership NHS Foundation Trust, the National Ethics Research Service Northwest – Haydock, and The University of Reading Research Ethics Committee.

**What if there is a problem?**
*Complaints*
If you have a concern about any aspect of this study, you should ask to speak to Professor Hill and Dr Helen Sharp or a member of their research team who will do their best to answer your questions. If they are unable to resolve your concern or you wish to make a complaint regarding the study, please contact the Head of the School of Psychology and Clinical Language Sciences, Professor Laurie Butler on 0118 378 5743 or by email to l.t.butler@reading.ac.uk

*Harm*
In the event that something does go wrong and you or your child are harmed during the research you may have grounds for a legal action for compensation against The University of Reading and The University of Liverpool but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

**Further information and contact details:**
When the researcher meets you they will be very happy to answer any questions you might have. In the meantime, if you would like any more information, please do not hesitate to contact Professor Jonathan Hill, Dr Helen Sharp or Liz Green / Karen Rafferty (study administrators) on the freephone number shown on the front page.

Appendix 3: Supplementary analysis on stability of CU from, age 2.5 to 5 years

| | Present sample[a] | Frick et al. 2003[b] (4 time points over 4 years, 98 children selected by CU and CP scores) | Barry et al. 2008[c] (3 time points over 3 years, 80 children selected on aggression scores) |
|---|---|---|---|
| Time 1 to time 2 | .74 | .76 | .72 |
| Time 1 to time 3 | .64 | .87 | .76 |
| Time 2 to time 3 | .63 | Don't report | .77 |
| Time 1 to time 4 | n/a | .80 | n/a |
| Overall stability | .78 | .90 | .83 |

*Note.* Intra-class correlations using absolute agreement, average measures. [a]Time 1 = age 2.5 years, time 2 = age 3.5 years, time 3 = age 5 years. [b]Time 1 = Third grade (age 8-9 years), time 2 =fourth grade (age 9-10 years), time 3 = fifth grade (age 11-12 years), time 4 = fifth grad (age 12-13 years). [c]Time 1 = fourth grade (age 9-10 years), time 2 = fifth grade (age 11-12 years), time 3 = sixth grade (age 12-13 years).

*References*

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Frick, P. J., Kimonis, E. R., Dandreaux, D. M., & Farell, J. M. (2003). The 4 year stability of psychopathic traits in non-referred youth. *Behavioral sciences & the law*, *21*(6), 713-736.